BONE

Anatomy & Physiology I

Key Points

- Differences between cartilage & bone
- Composition and types of cartilage
- The relationship of periosteum to compact bone.
- Composition of bone & homeostasis
- Stimulating bone growth in the prepubertal adolescent.

Key Points

- The types of synovial joint
- Event that occurs in the breaking of a long bone & types of fractures

FUNCTIONS

- Structural support
- Protection
- Movement
- Mineral storage
- Hematopoiesis
- Energy storage

WHAT IS BONE

A connective tissue that consists of cells and fibers embedded in a calcified ground substance

COMPARISON TO CARTILAGE

- Similar in that both have:
  - Cells and ground substance
  - CT covering
  - Appositional & interstitial growth
- Differ in that:
  - Bone has mineralized matrix
  - Bone is vascularized (nutrition)
  - Cavities in some bone
  - Bone has high metabolic rate

BONE CELLS

- Stem (osteoprogenitor) cells
- Osteoblasts
  - Immature, secreting cells
- Osteocytes
  - Mature; found in lacunae
- Osteoclasts
  - Multinucleated cells
  - Resorb calcified bone

BONE MATRIX

- Collagen fibers
- Calcified ground substance - *hydroxyapatite*
  - Calcium phosphate
  - Calcium carbonate
- Proteins
- Osteoid - organic matrix, ground substances & collagen fibers

BONE MATRIX

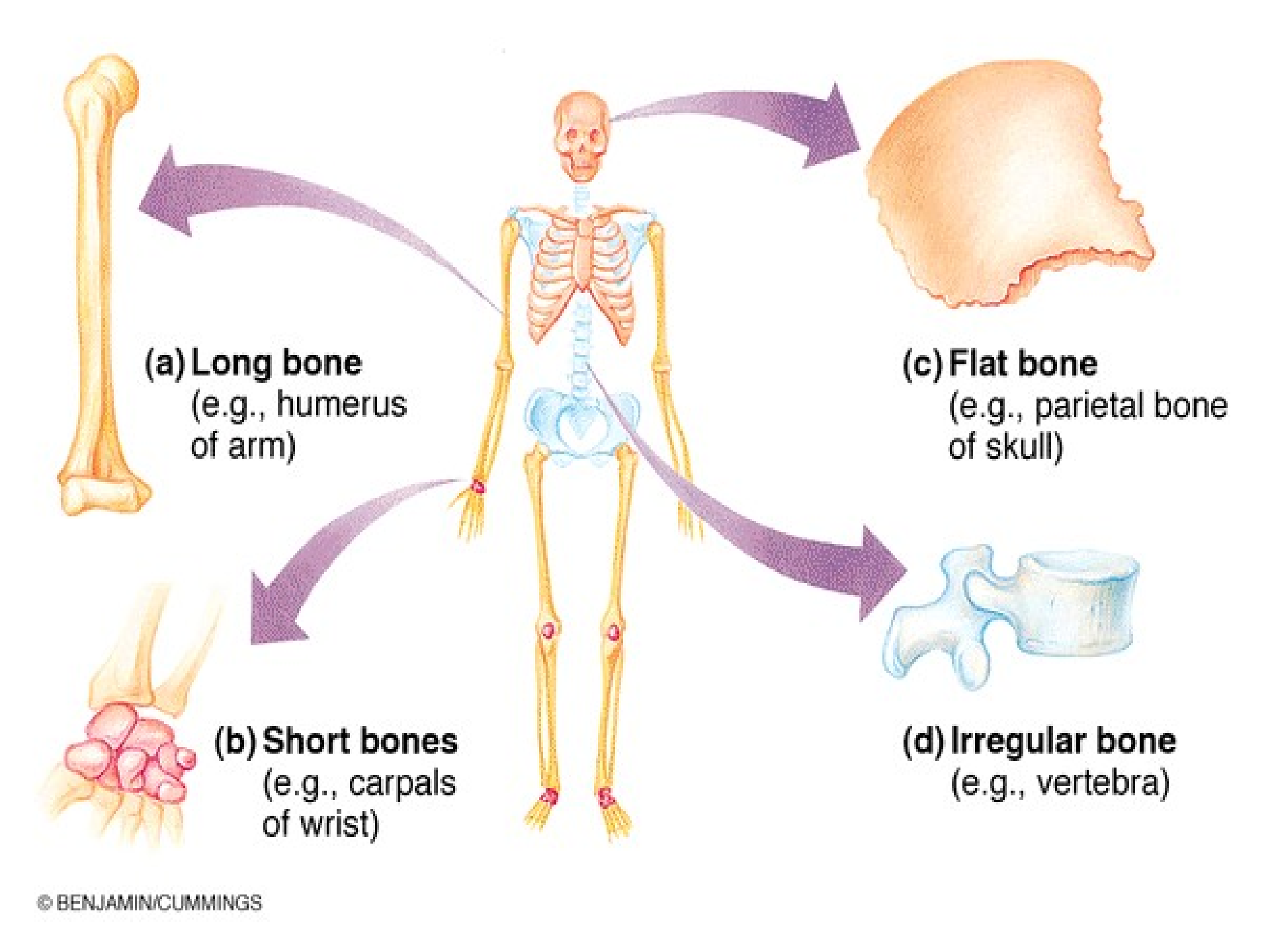
- Calcification or mineralization
  - osteoblast deposit mineral salts on a framework formed by the collagen fibers of the matrix
  - mineral salts crystalize and the tissue hardens

BONE CHARACTERISTICS

- Hardness & Flexibility
  - Allows bone to rspond to mechanical stress from tension and compressive forces

SHAPES OF BONE

- Long bones
- Short bones
- Flat bones
- Irregular bones
- Sutural bones
- Sesamoid bones



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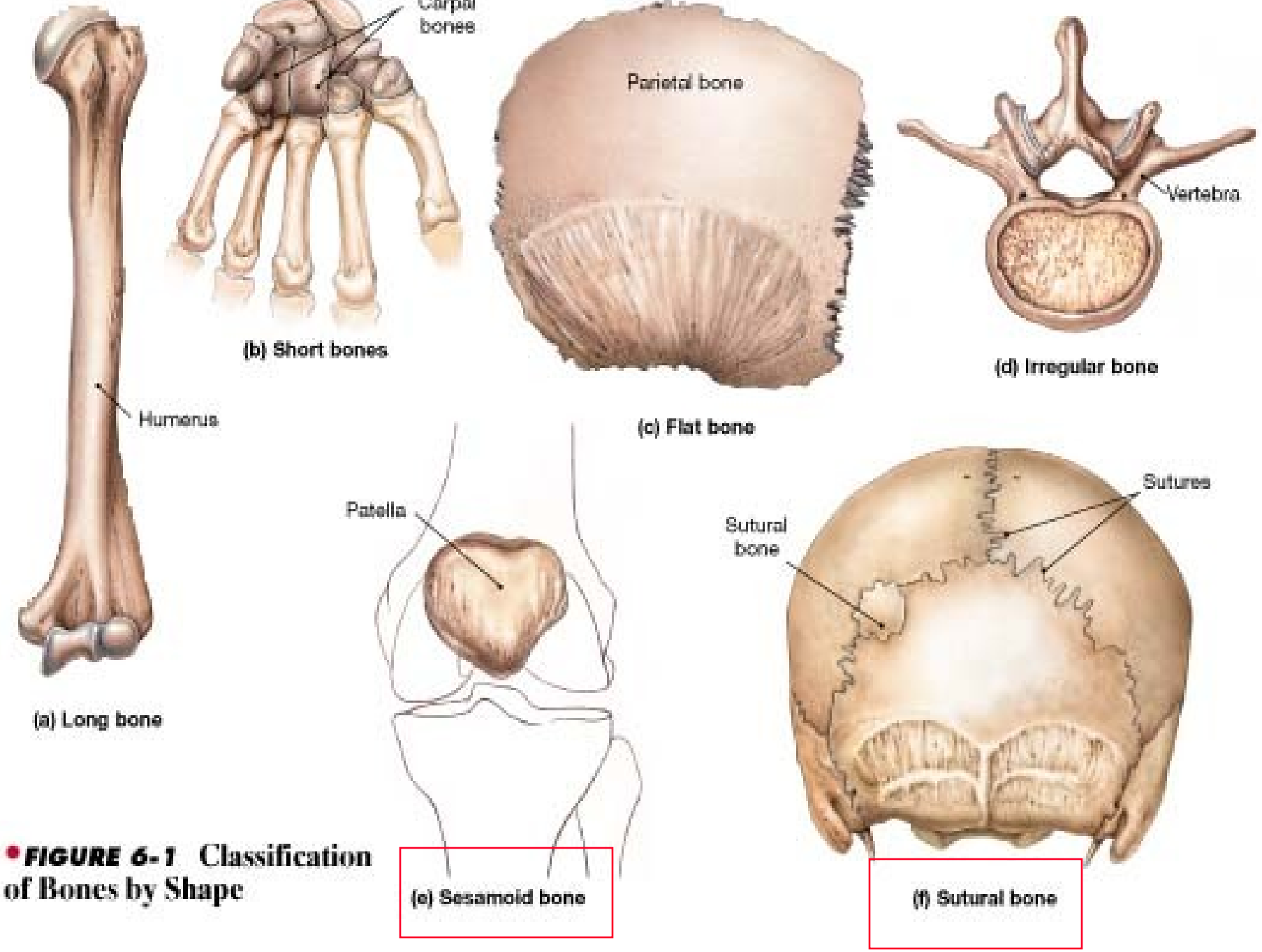


FIGURE 6-1 Classification of Bones by Shape

TYPES OF BONE

- Compact bone
  - Dense, lamellar organization
  - Interstitial bone
- Spongy bone
  - Trabecular meshy appearance
  - Cancellous bone

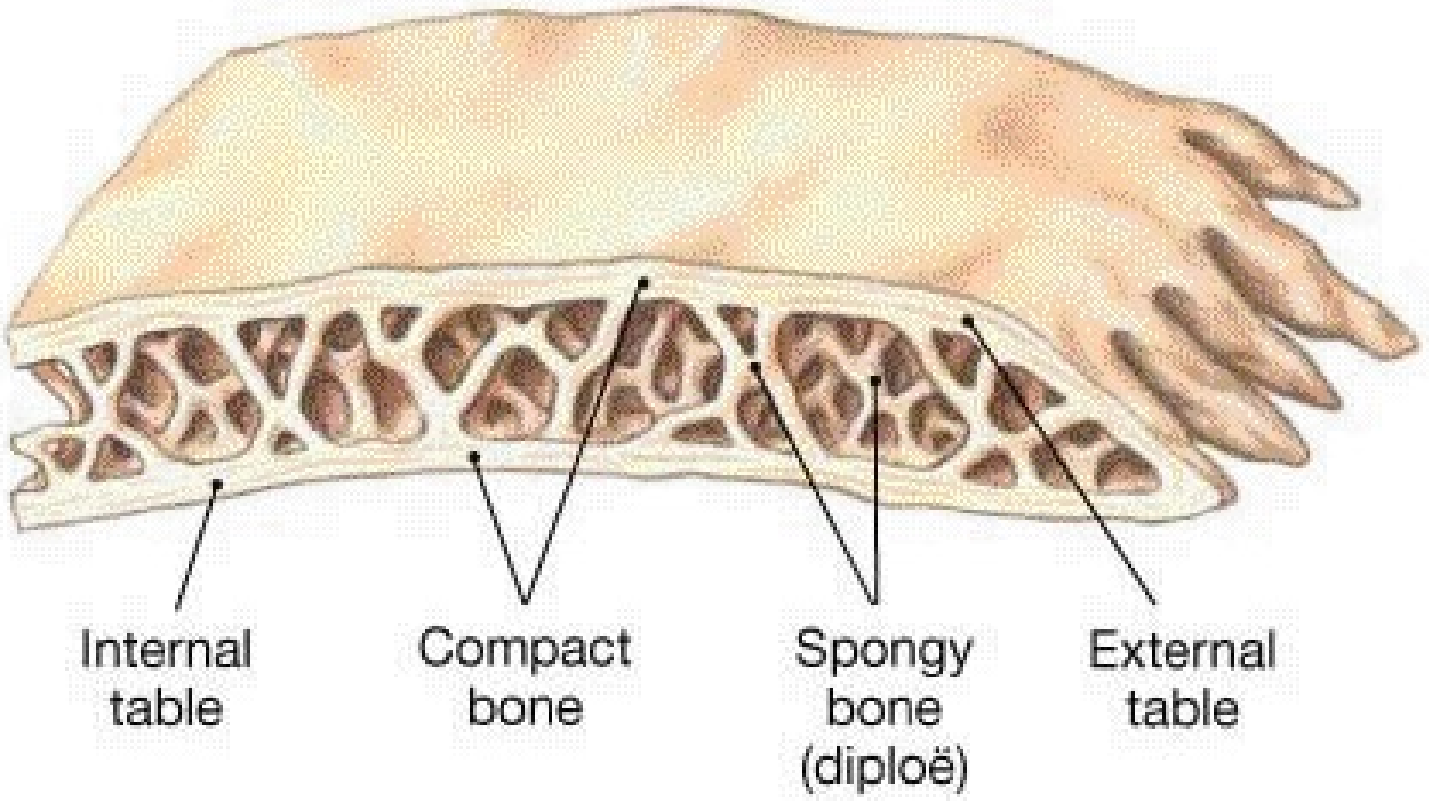
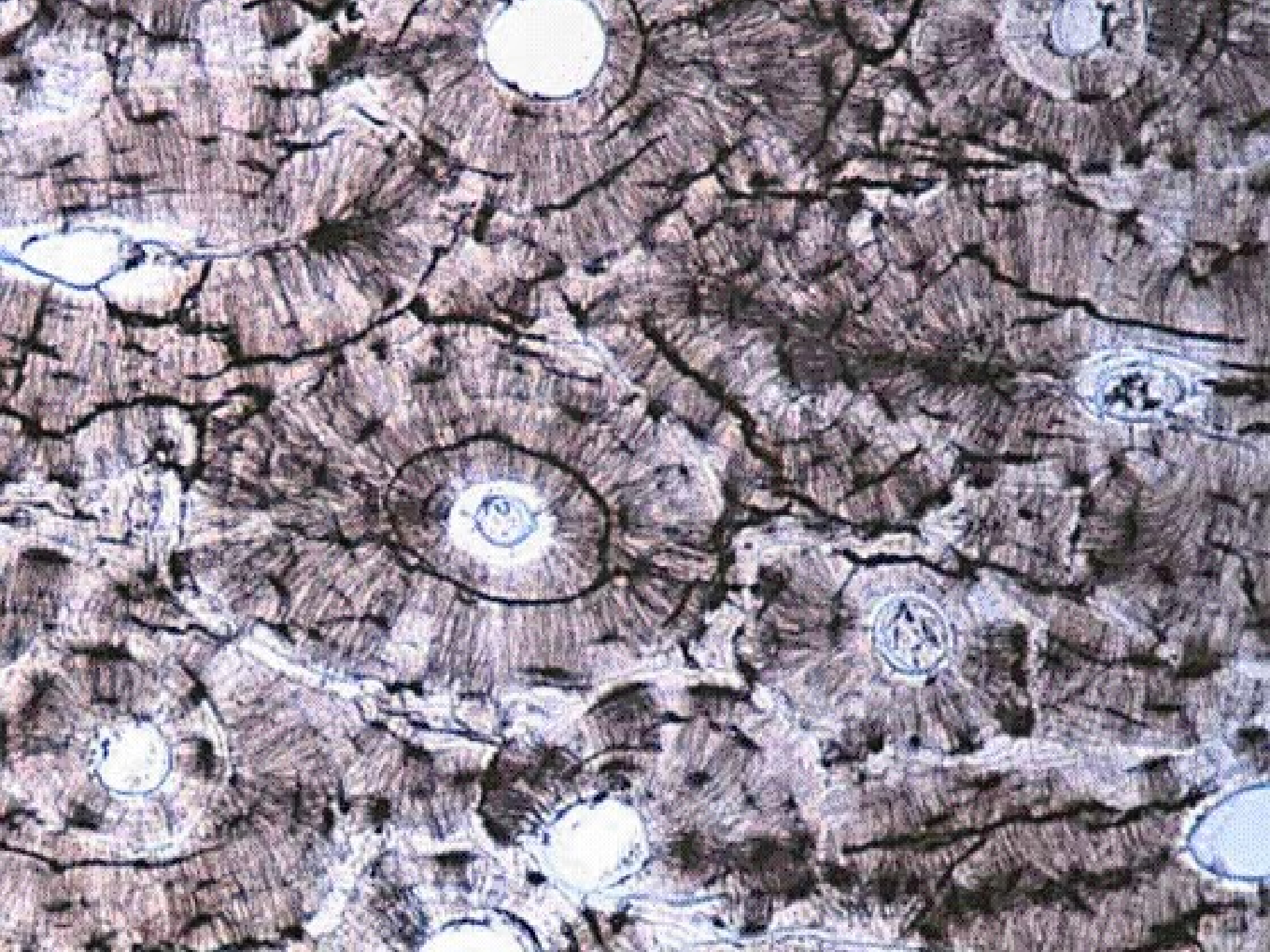


FIGURE 6-2 Bone Structure. **(b)** Structure of a flat bone.

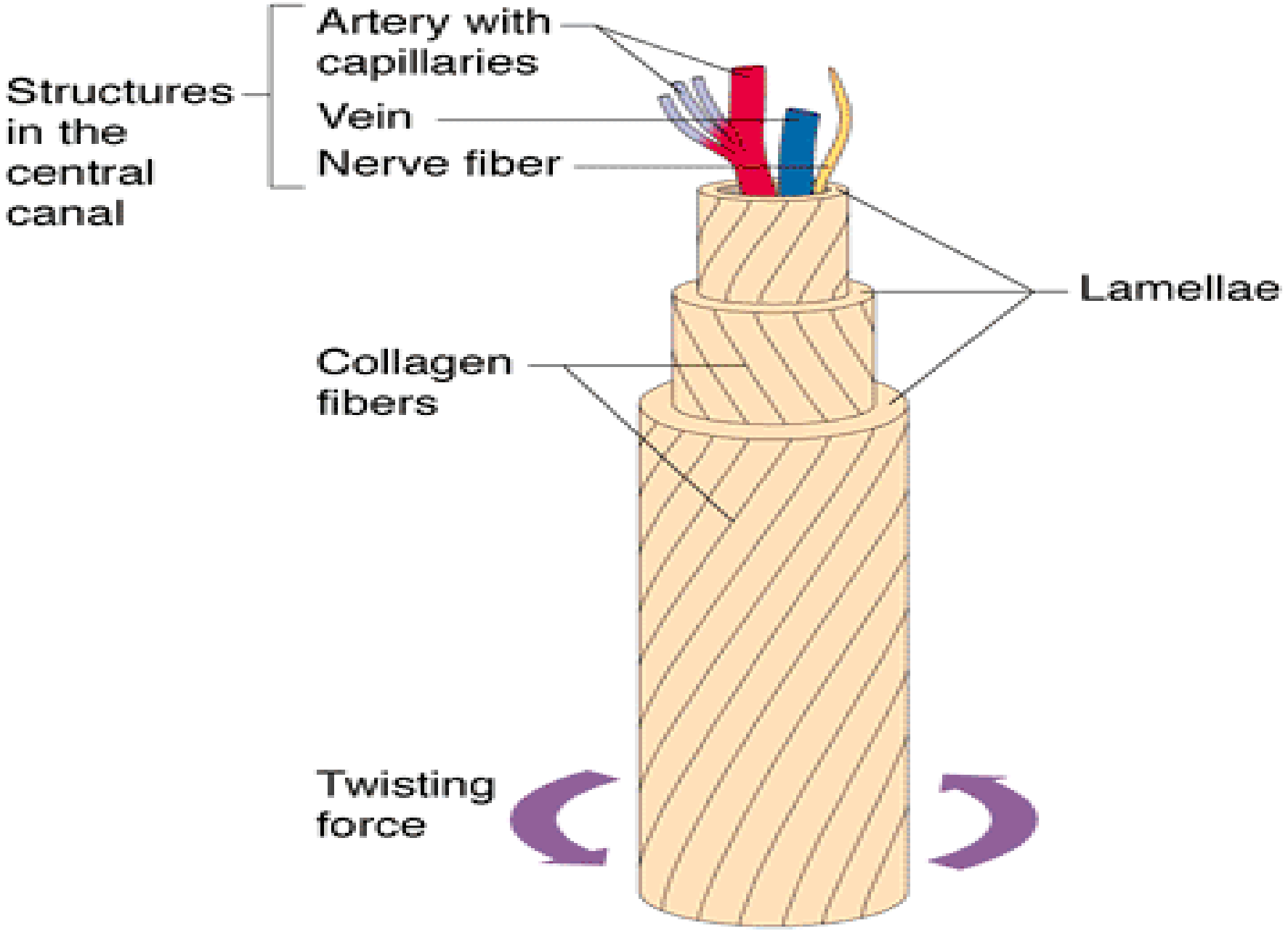
COMPACT BONE

- Volkmann’s canals
- Haversian (central) canals
- Concentric lamellae
- Lacunae
- Canaliculi



HAVERSIAN SYSTEM

- Also called an OSTEON
- The functional unit of bone is the Osteon which consists of:
  - A Central canal & branching canals
  - Surrounding lamellae
  - Osteocytes in their Lacunae
  - Canaliculi



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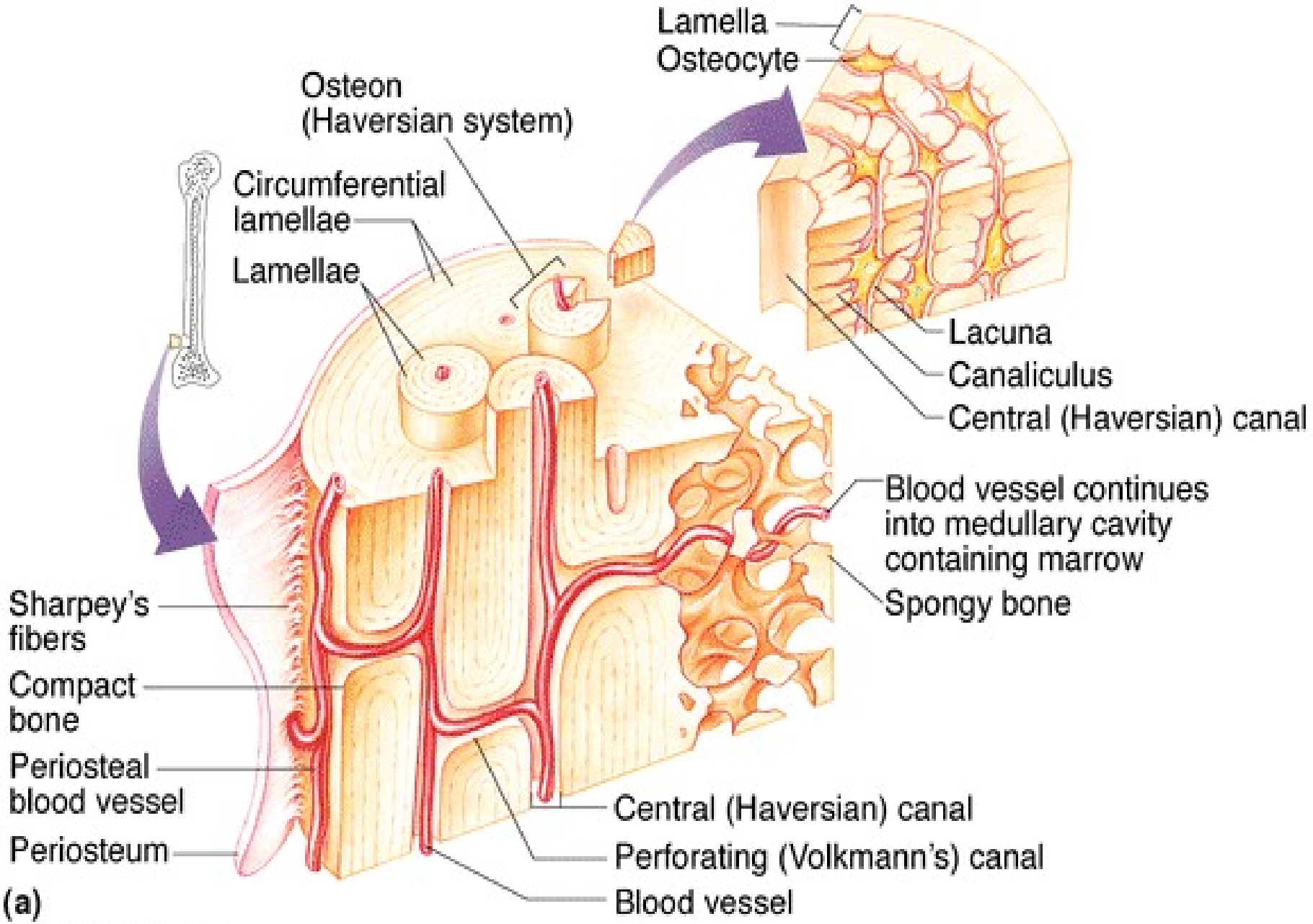

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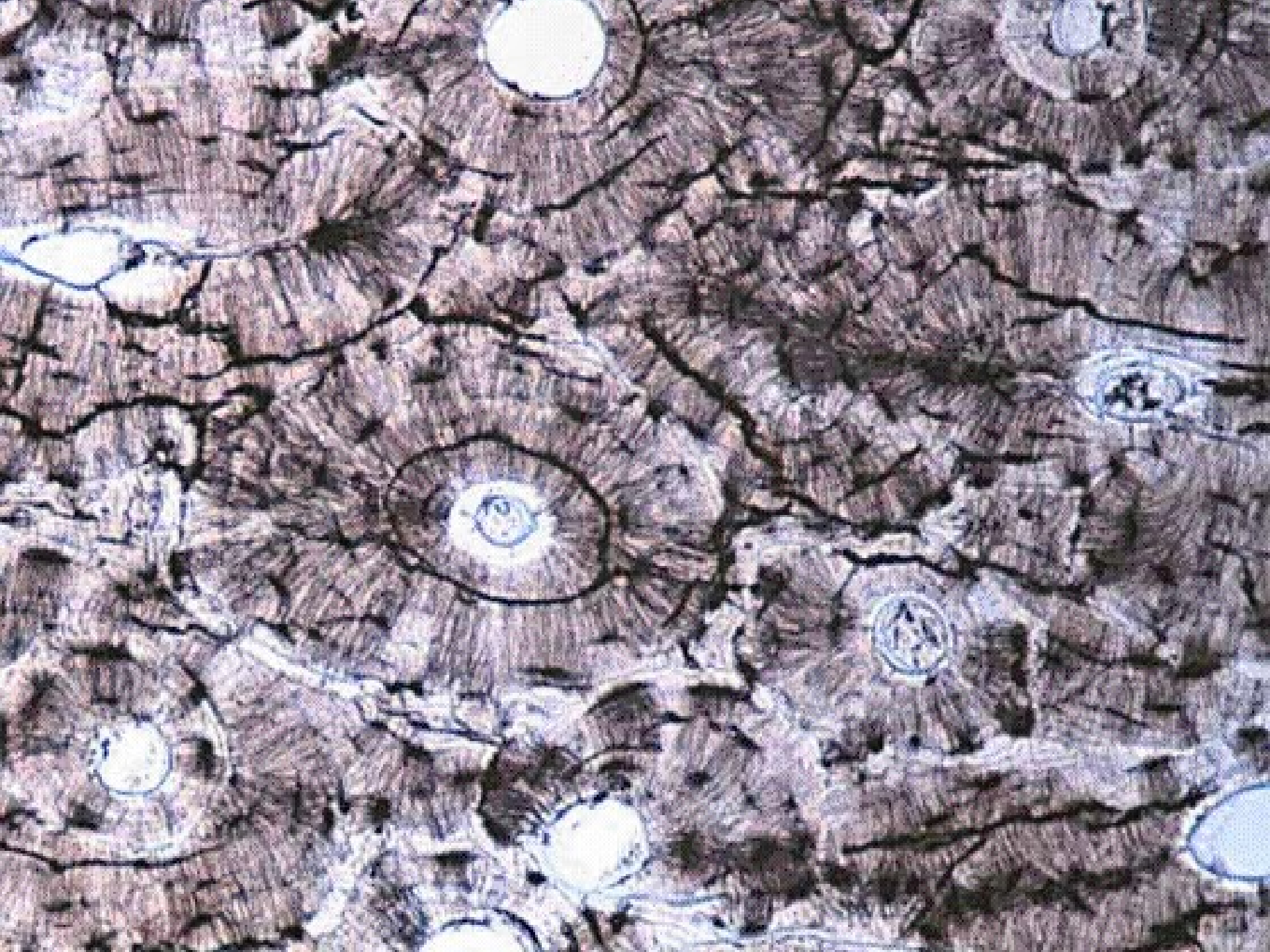


ENDOSTEUM

- Lines medullary (marrow) cavity
- Mainly cellular; few fibers

GROSS STRUCTURE

- Diaphysis: shaft
- Epiphysis: ends
- Metaphysis: area of bone growth
  - Epiphyseal plate
  - Epiphyseal line
- Periosteum lines outside
- Cavity
  - Endosteum

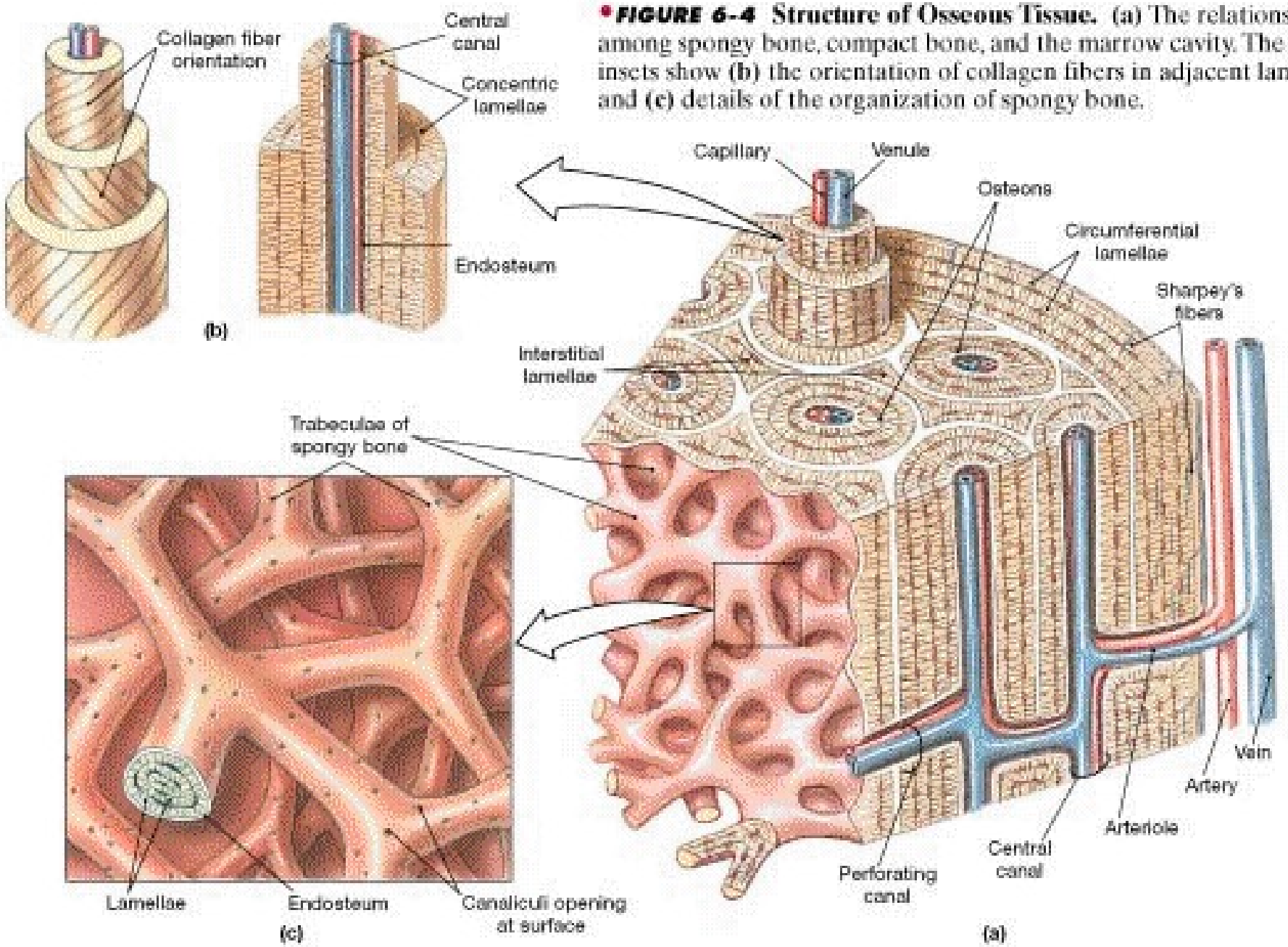


FIGURE 6-4 Structure of Osseous Tissue. (a) The relationships among spongy bone, compact bone, and the marrow cavity. The insets show (b) the orientation of collagen fibers in adjacent lamellae and (c) details of the organization of spongy bone.

PERIOSTEUM

- Dense, fibrous CT
- Contains stem cells
- Contains NAVL
- Attach tendons, ligaments
- Site for growth and repair

The endosteum (below) is an incomplete cellular layer. It contains epithelial cells, osteoblasts, osteoprogenitor cells, and osteoclasts.

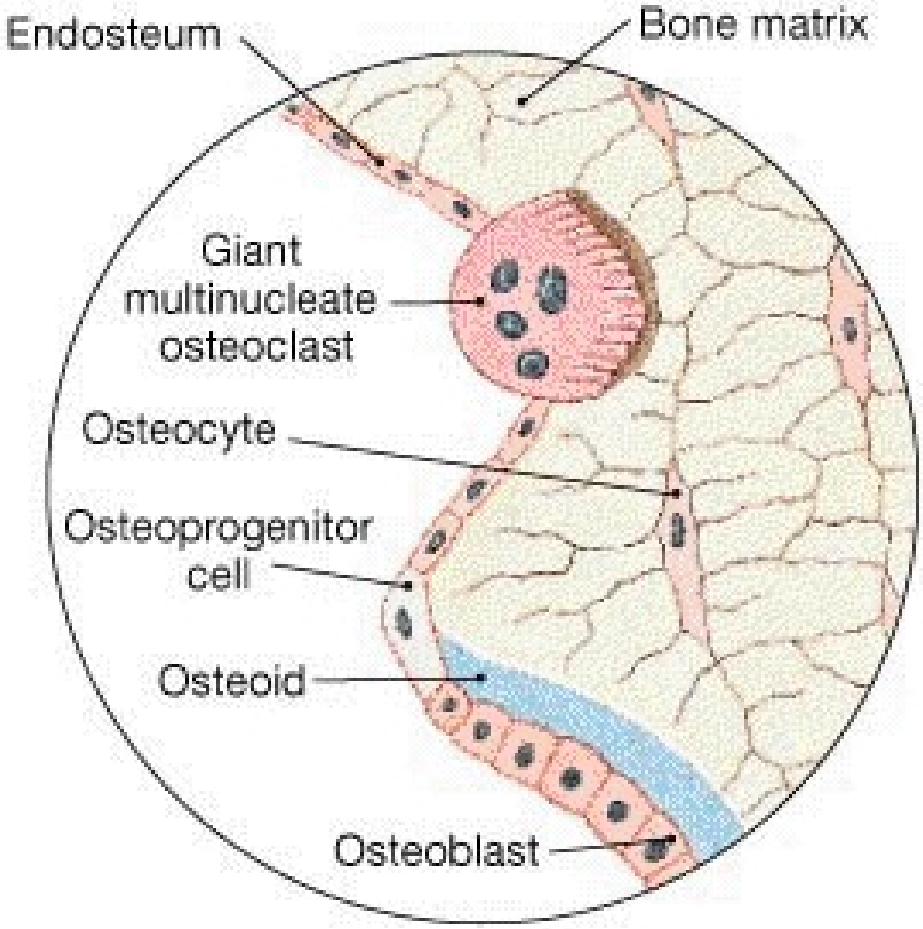
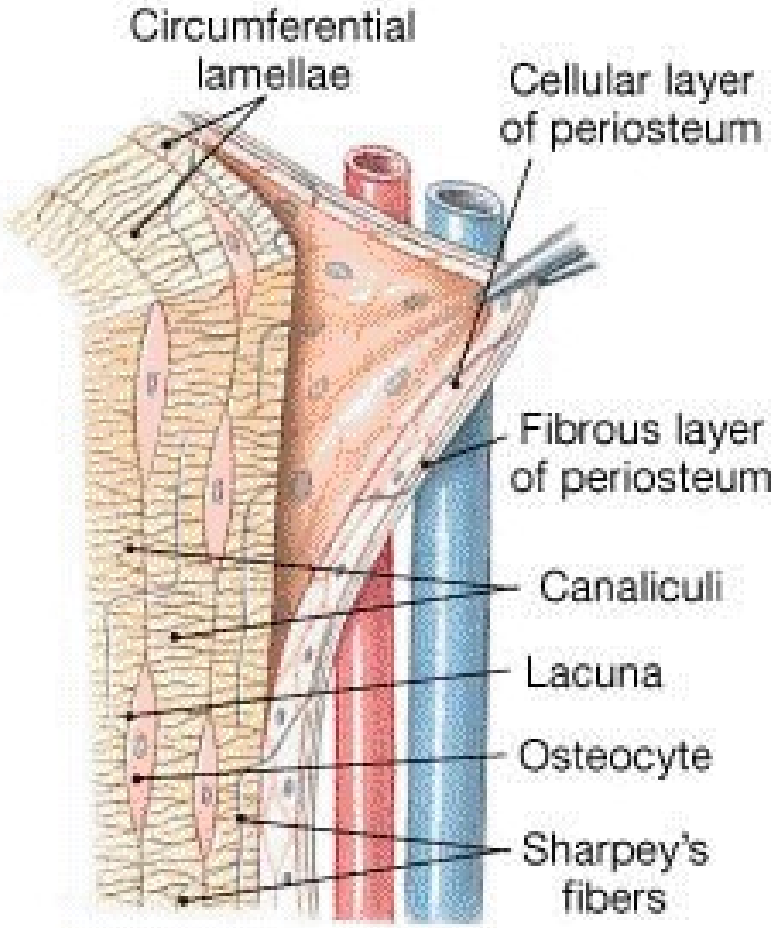


FIGURE 6-6 The Endosteum and Periosteum



The periosteum contains outer (fibrous) and inner (cellular) layers. Collagen fibers of the periosteum are continuous with those of the bone, adjacent joint capsules, and attached tendons and ligaments.

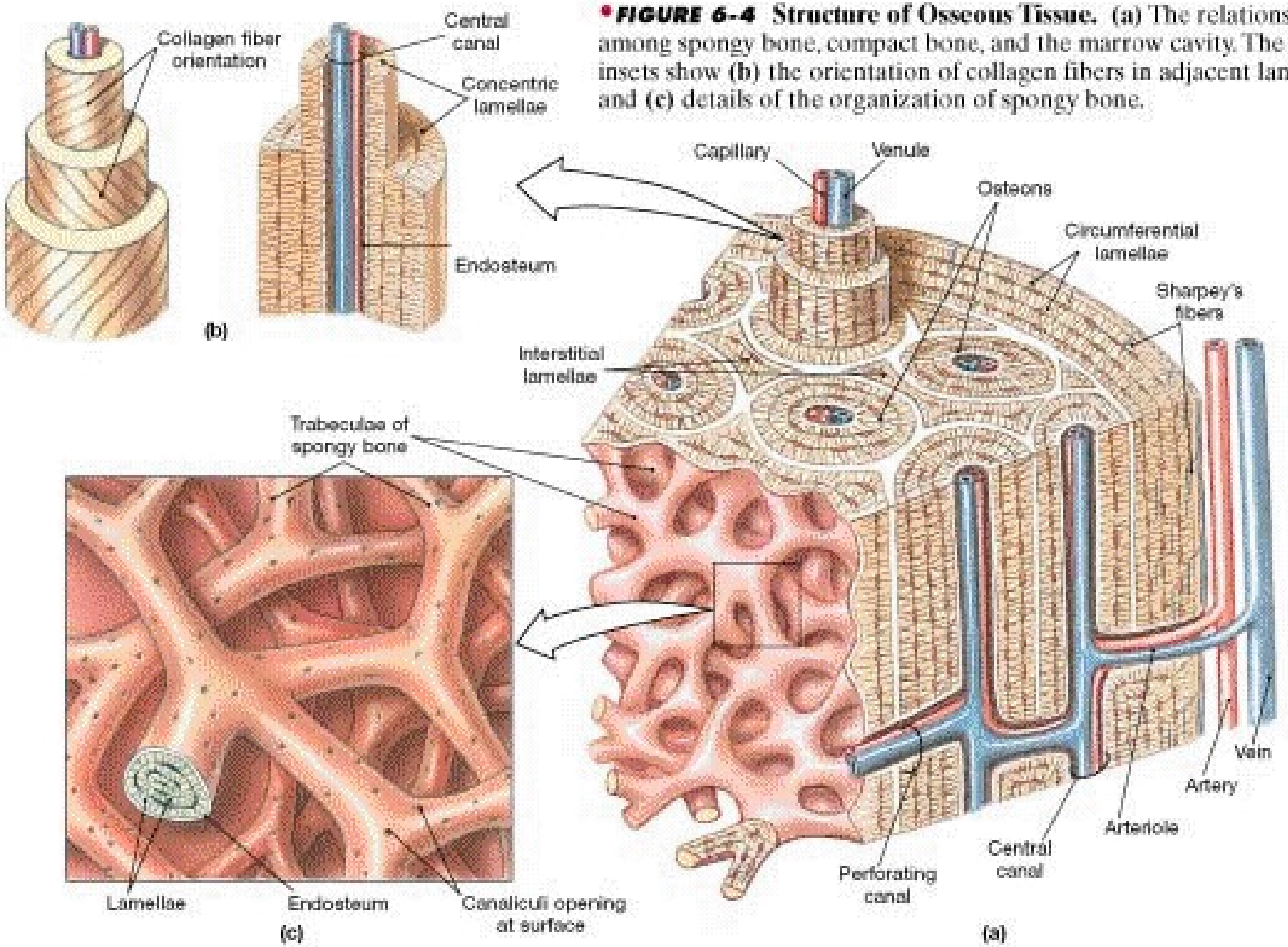
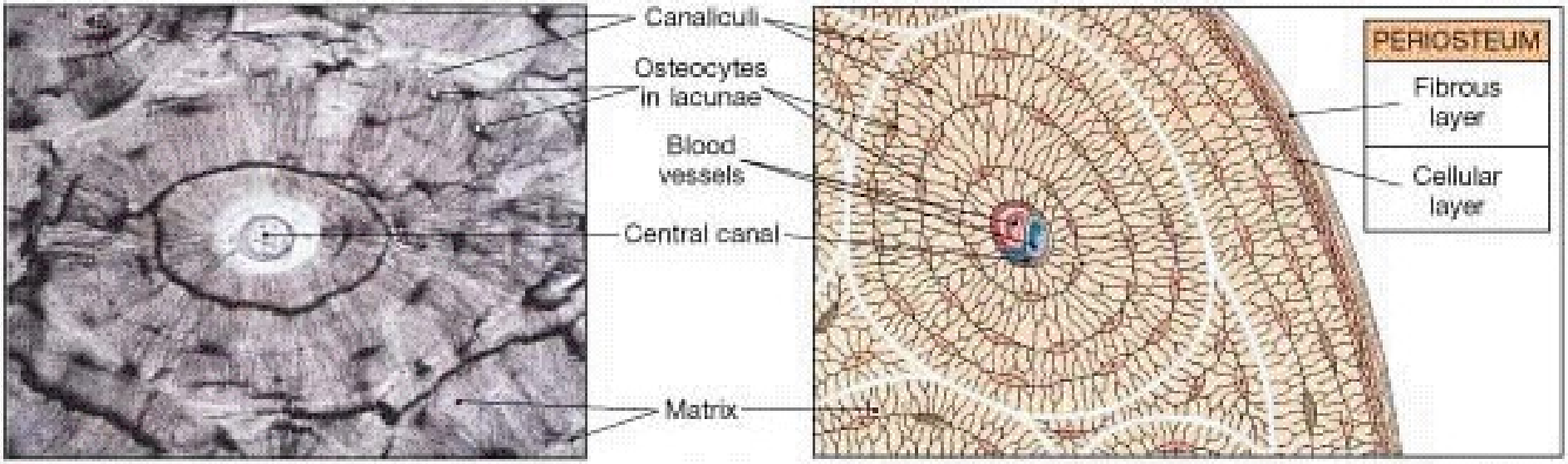
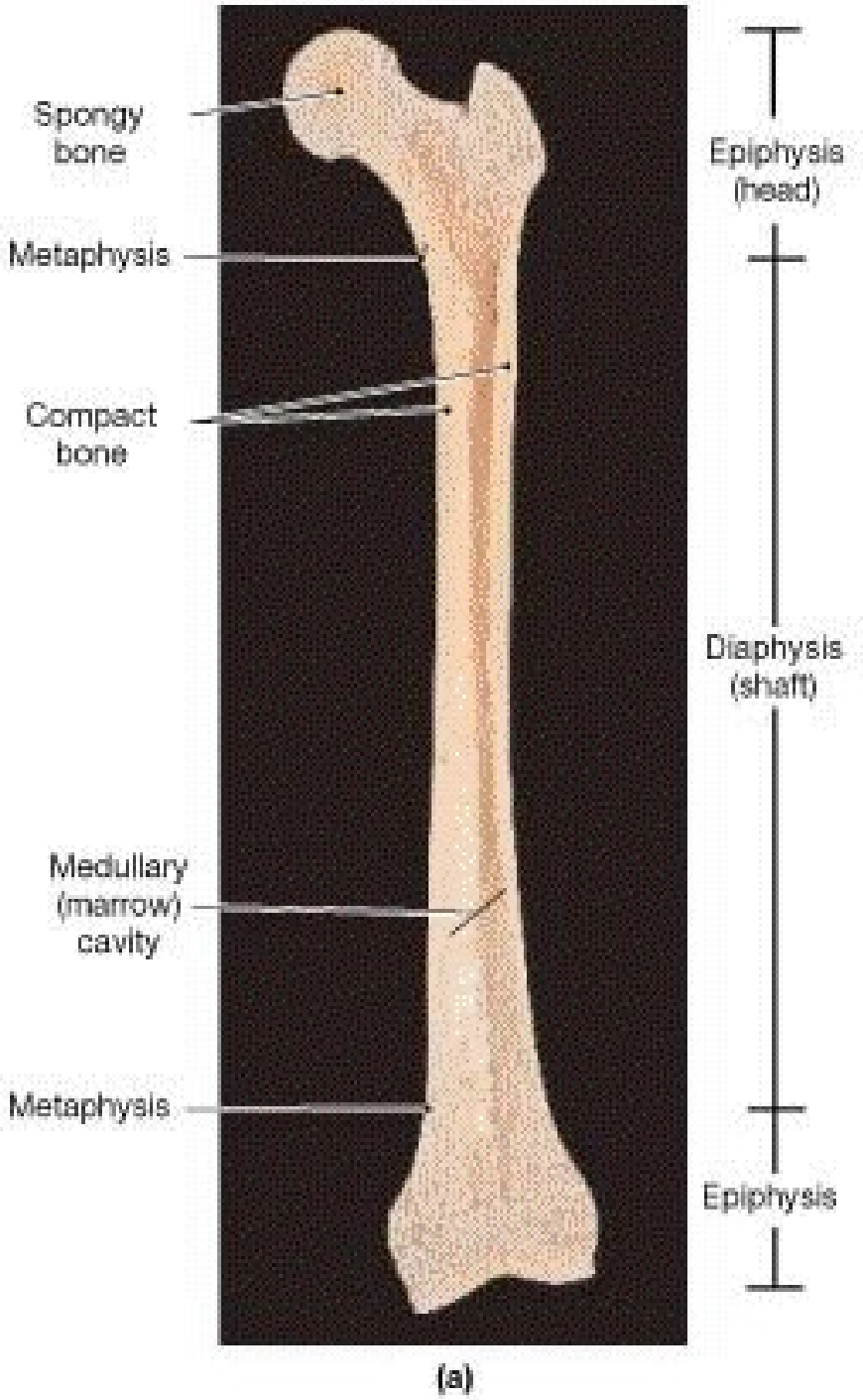


FIGURE 6-4 Structure of Osseous Tissue. (a) The relationships among spongy bone, compact bone, and the marrow cavity. The insets show (b) the orientation of collagen fibers in adjacent lamellae and (c) details of the organization of spongy bone.



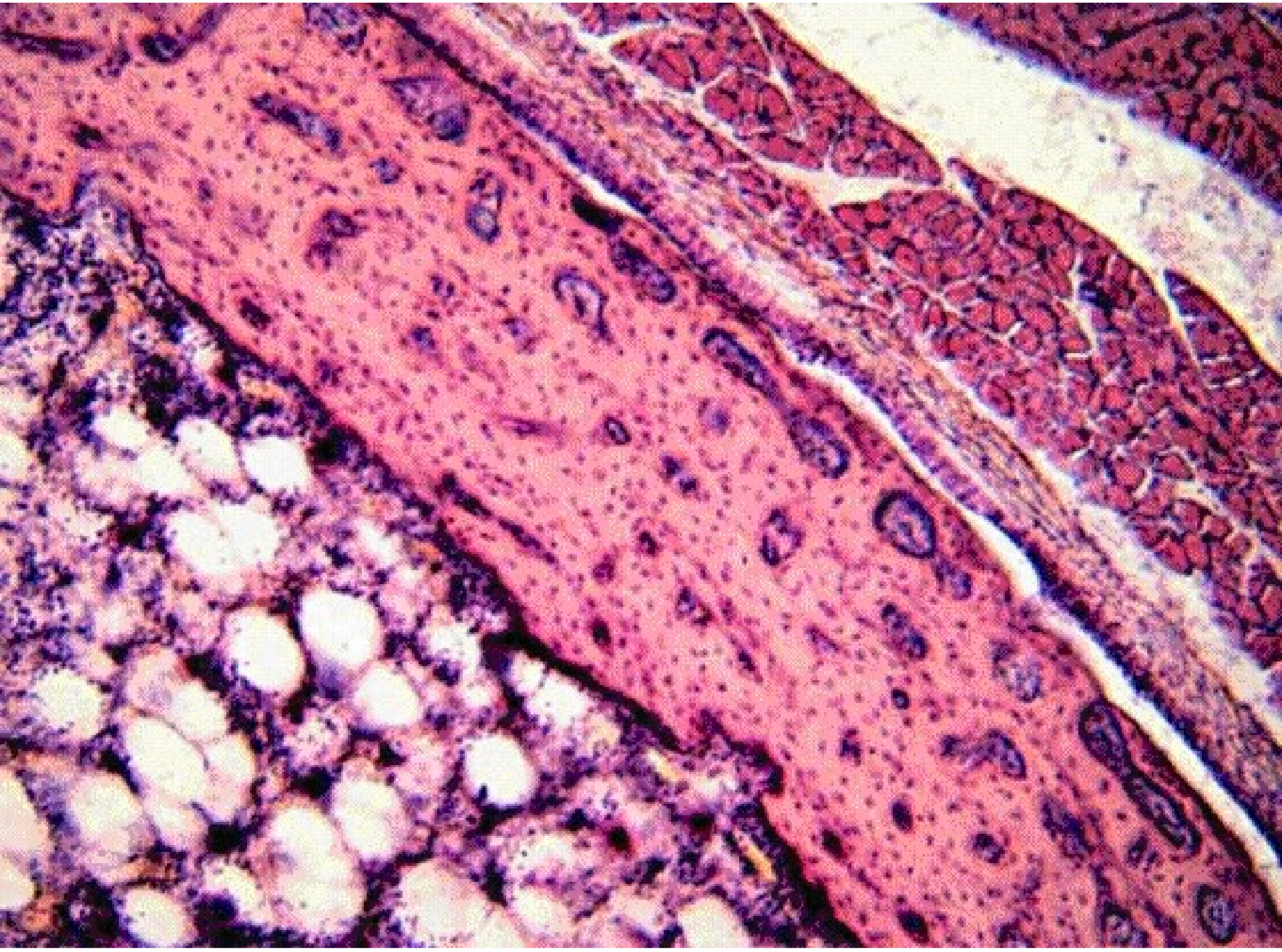
• ***FIGURE 4-14*** **Bone.** The osteocytes in bone are generally organized in groups around a central space that contains blood vessels. Bone dust produced during grinding fills the lacunae and the central canal, making them appear dark. (LM × 362)

FIGURE 6-2 Bone Structure.
(a) Structure of a representative long bone.



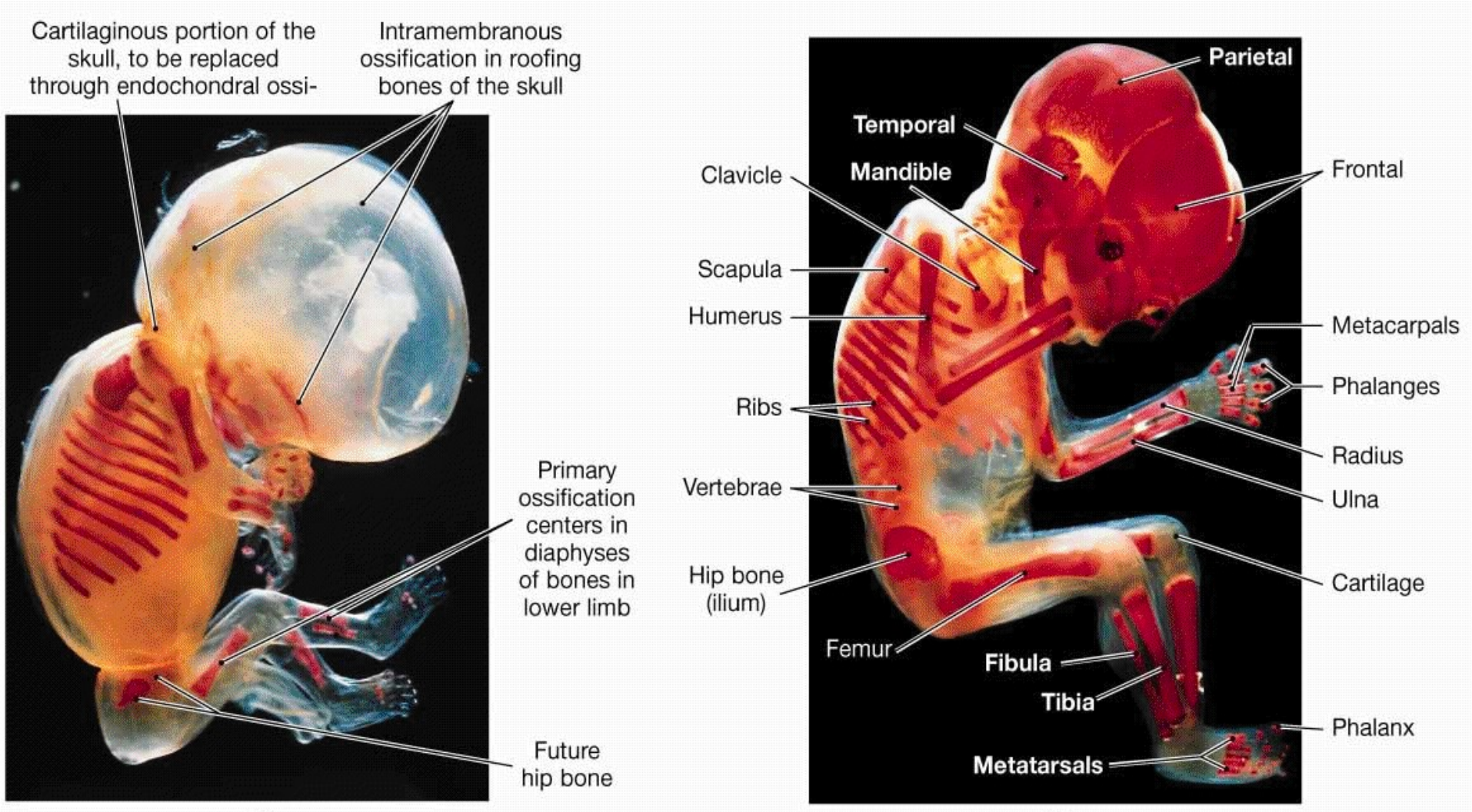
BONE MARROW

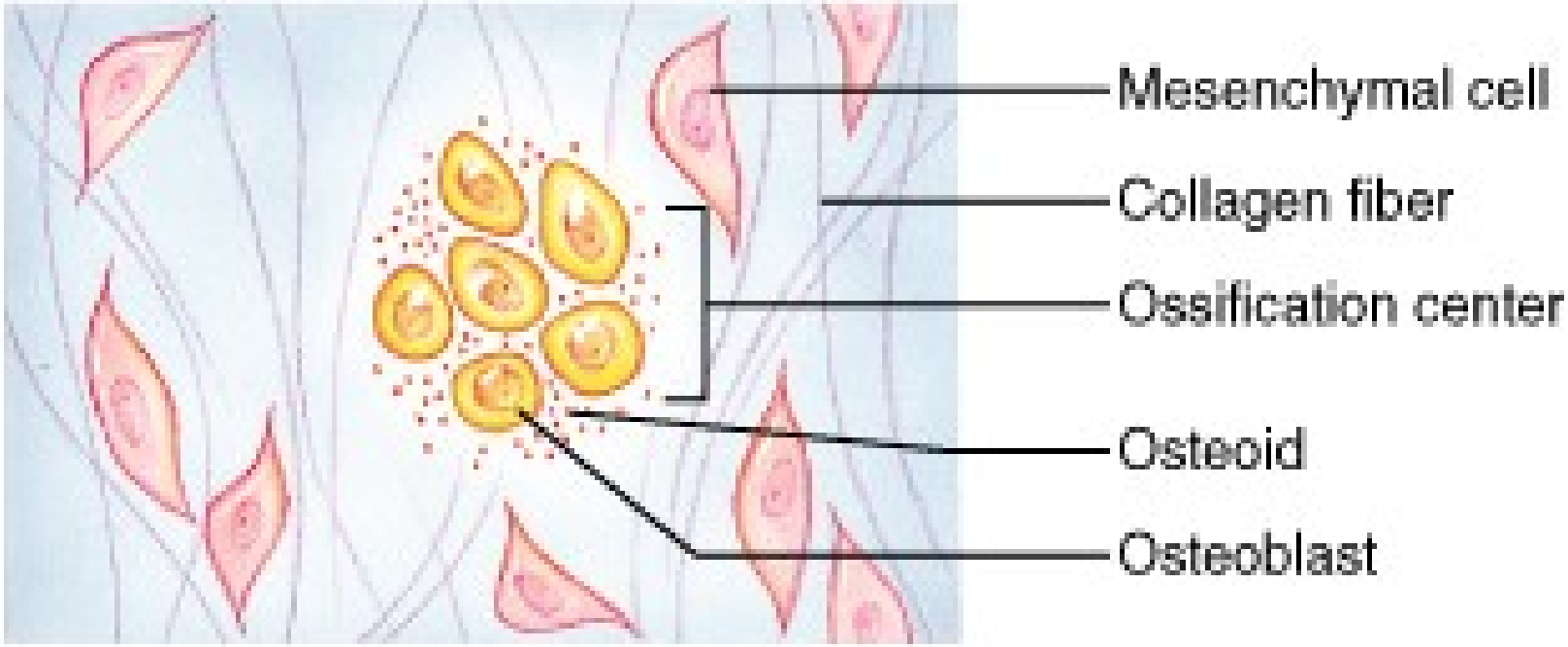
- Red marrow
  - Hemopoiesis
  - Mainly in long bones
- Yellow marrow
  - Inactive; reserve marrow
  - Found in long bones



BONE FORMATION

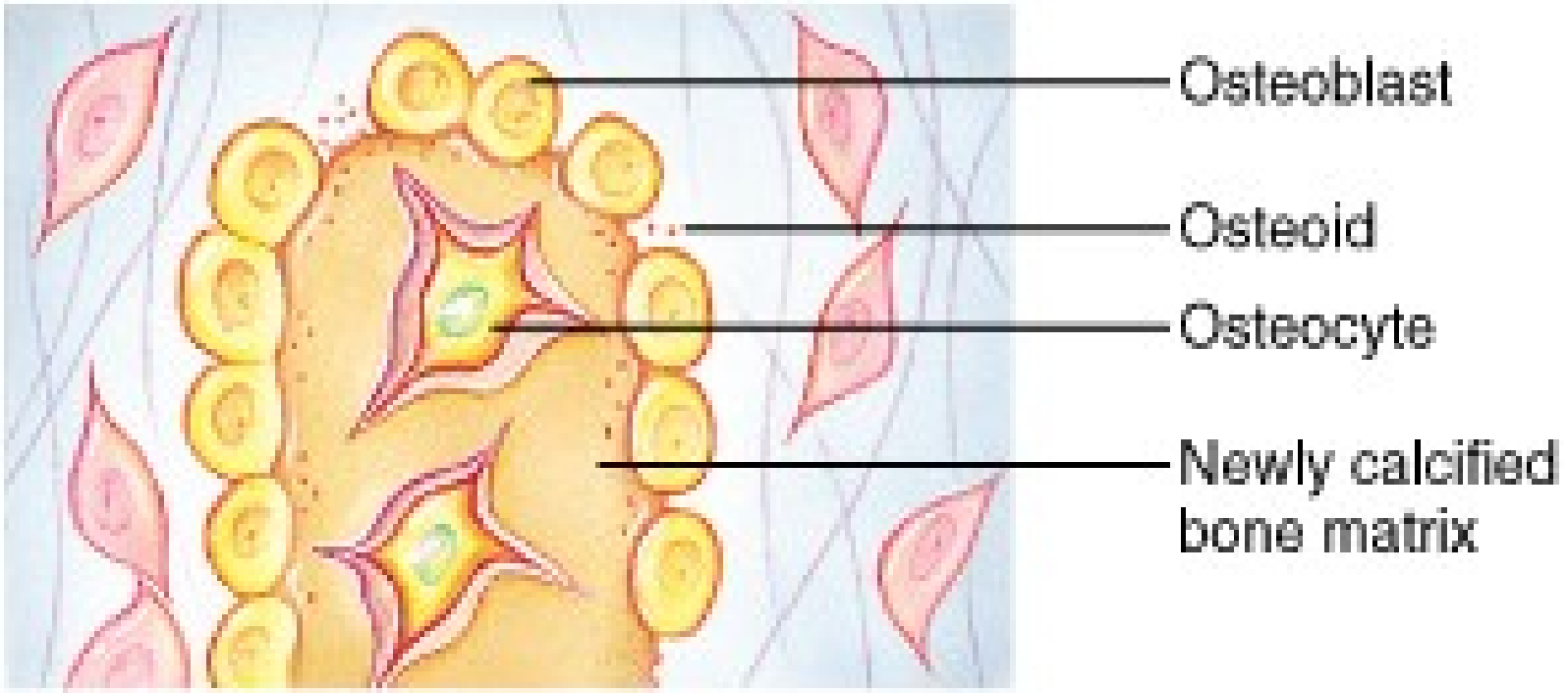
- **Intramembranous ossification**
  - Cells secrete bone in CT
  - Form spongy bone


Cartilaginous portion of the skull, to be replaced through endochondral ossi-
Intramembranous ossification in roofing bones of the skull
Primary ossification centers in diaphyses of bones in lower limb
Future hip bone
Parietal
Temporal
Mandible
Clavicle
Frontal
Scapula
Humerus
Metacarpals
Phalanges
Ribs
Radius
Ulna
Vertebrae
Hip bone (ilium)
Cartilage
Femur
Fibula
Tibia
Phalanx
Metatarsals



① **An ossification center appears in the fibrous connective tissue membrane.**

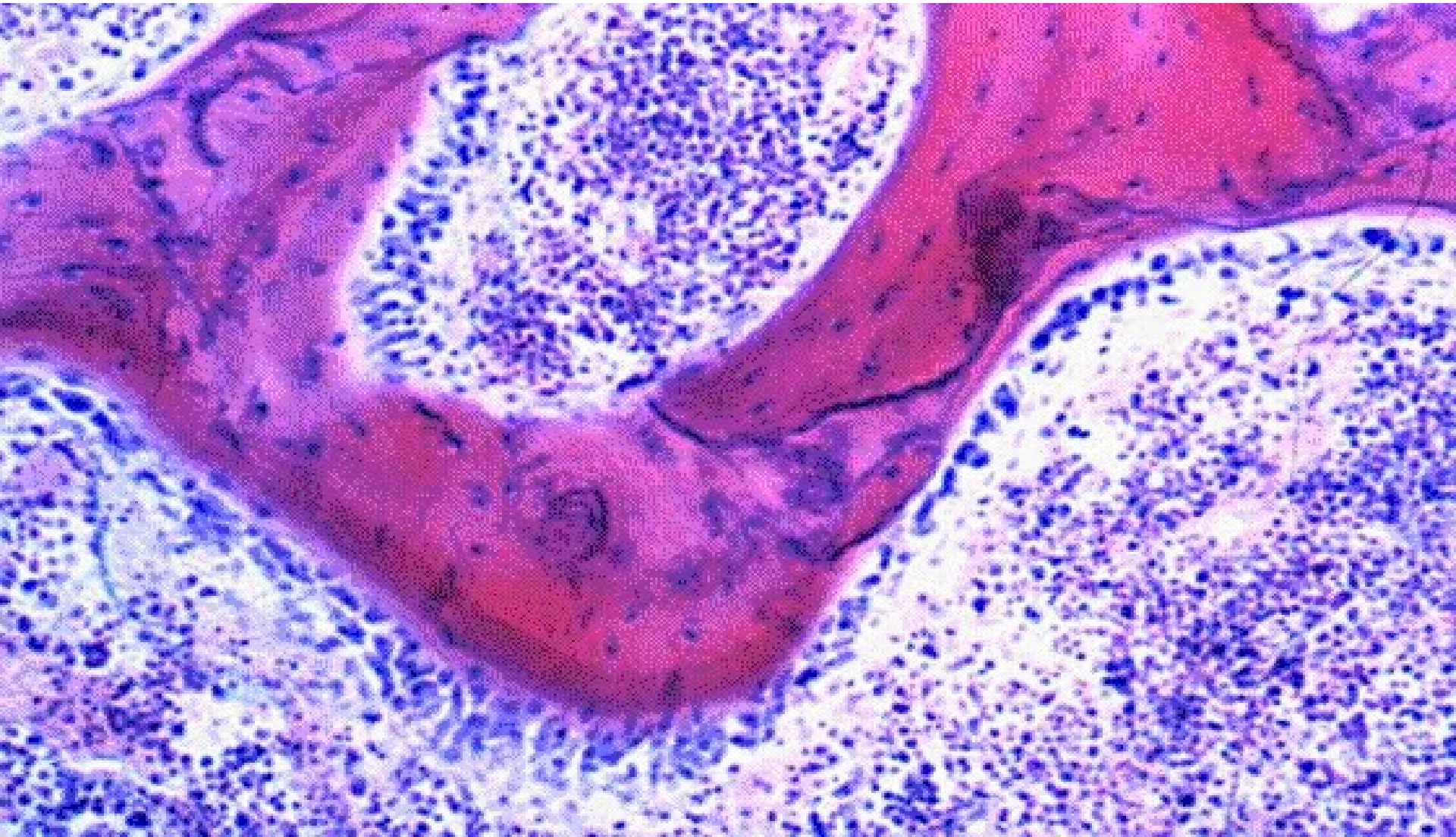
- Selected centrally located mesenchymal cells cluster and differentiate into osteoblasts, forming an ossification center.

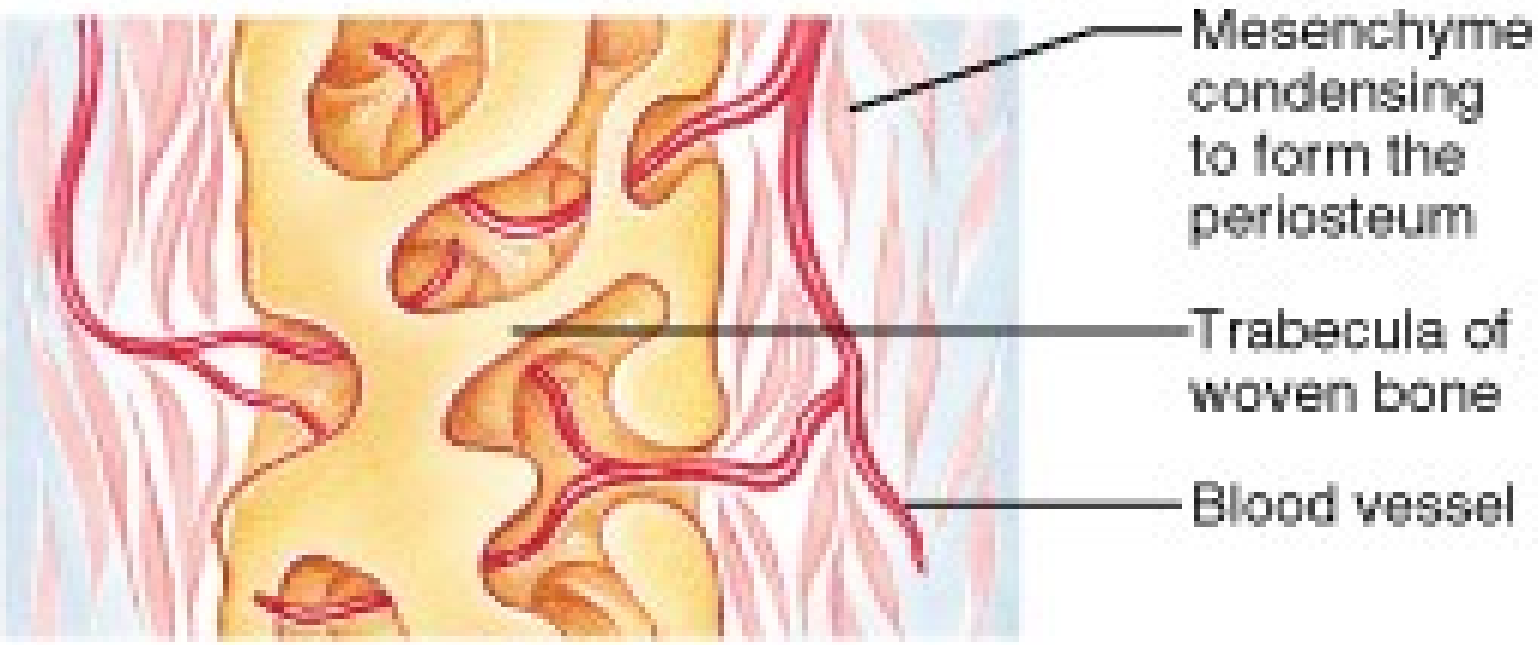


② **Bone matrix (osteoid) is secreted within the fibrous membrane.**

- Osteoblasts begin to secrete osteoid, which is mineralized within a few days.
- Trapped osteoblasts become osteocytes.

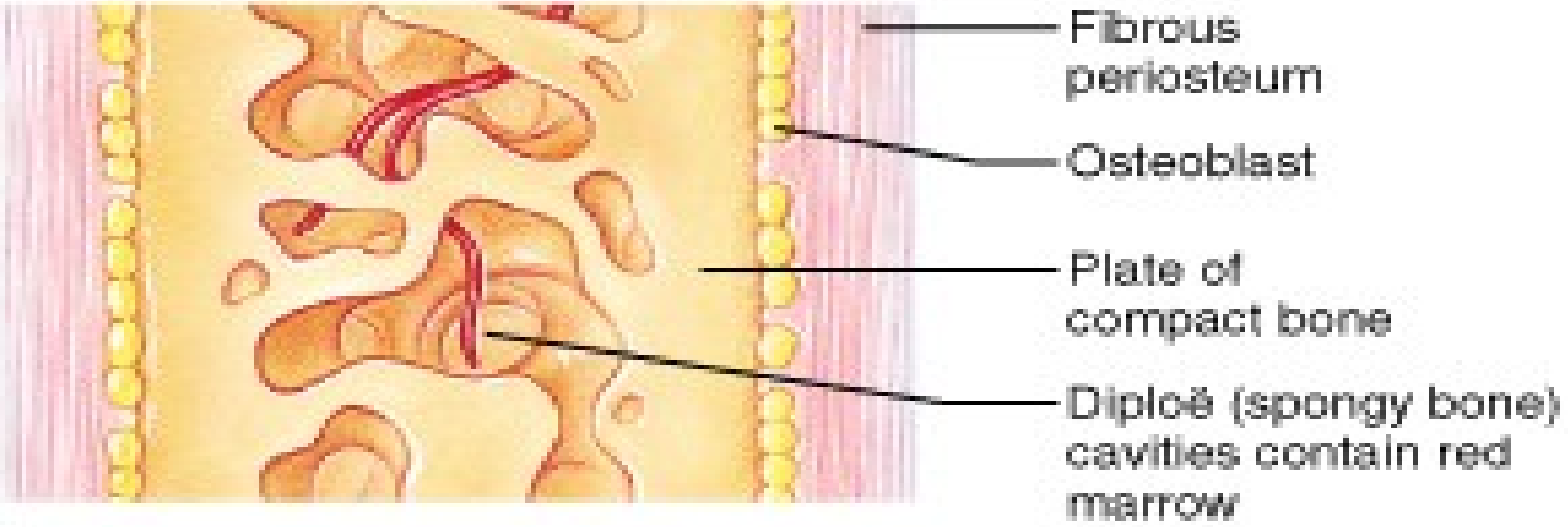
INTRAMEMBRANOUS OSSIFICATION





③ **Woven bone and periosteum form.**

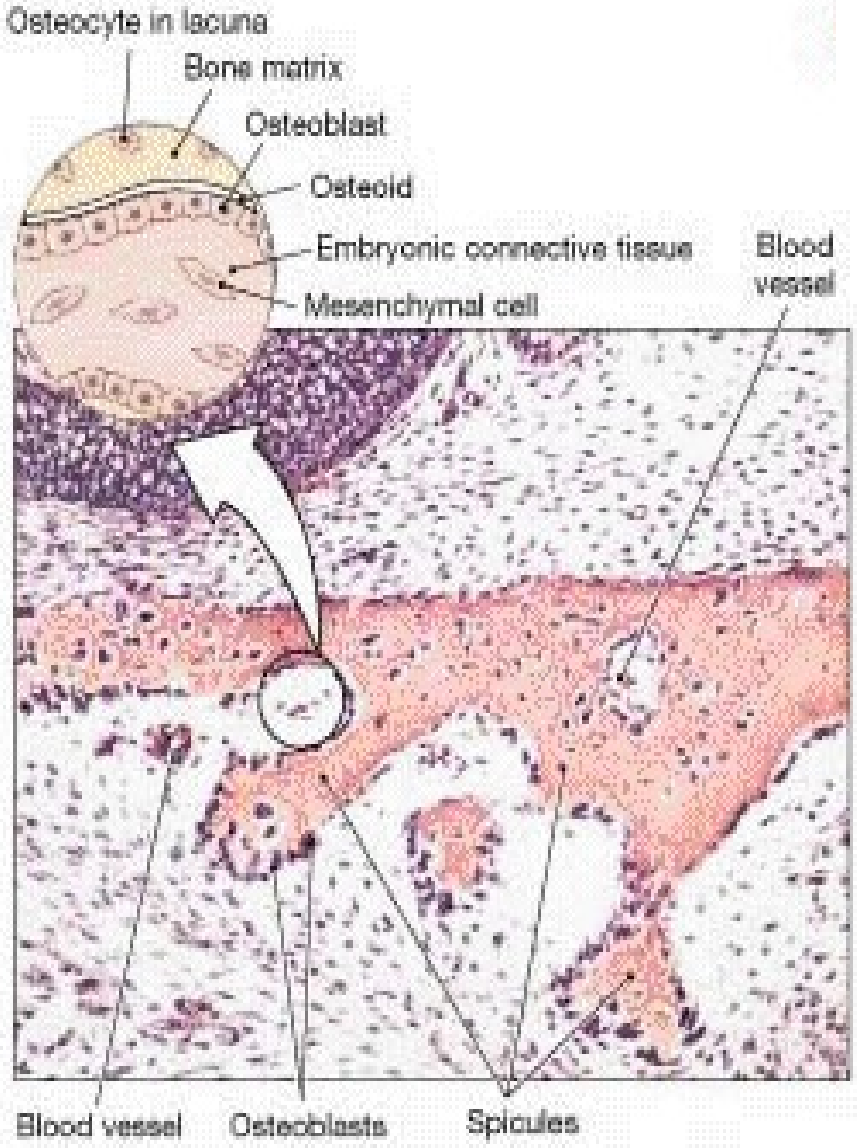
- Accumulating osteoid is laid down between embryonic blood vessels, which form a random network. The result is a network (instead of lamellae) of trabeculae (woven bone).
- Vascularized mesenchyme condenses on the external face of the woven bone and becomes the periosteum.



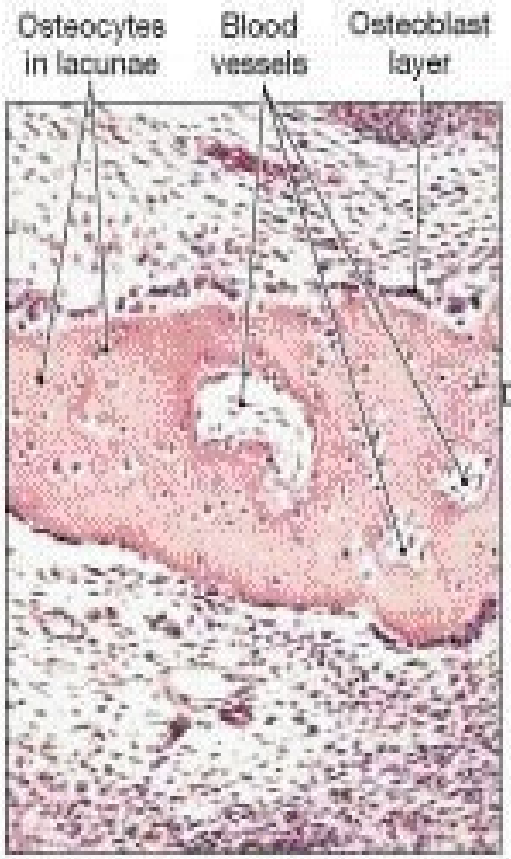
④ **Bone collar of compact bone forms and red marrow appears.**

- Trabeculae just deep to the periosteum thicken, forming a woven bone collar that is later replaced with mature lamellar bone.
- Spongy bone (diploë), consisting of distinct trabeculae, persists internally and its vascular tissue becomes red marrow.

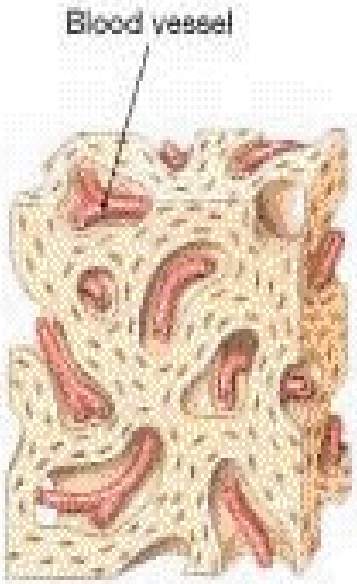
Intramembranous Ossification



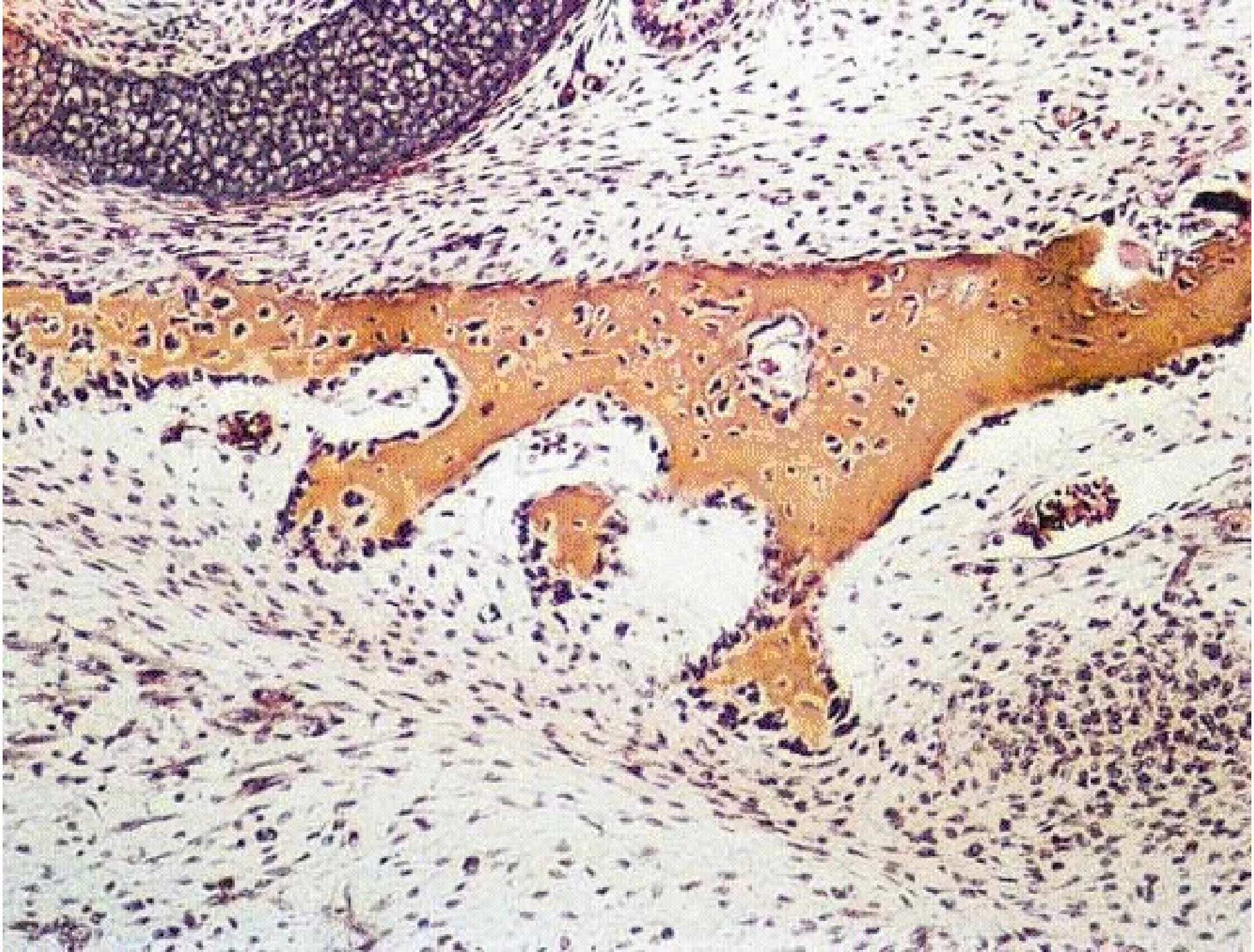
Step 1: Mesenchymal cells aggregate, differentiate, and begin the ossification process. The bone expands as a series of spicules that spread into surrounding tissues. (LM× 22)

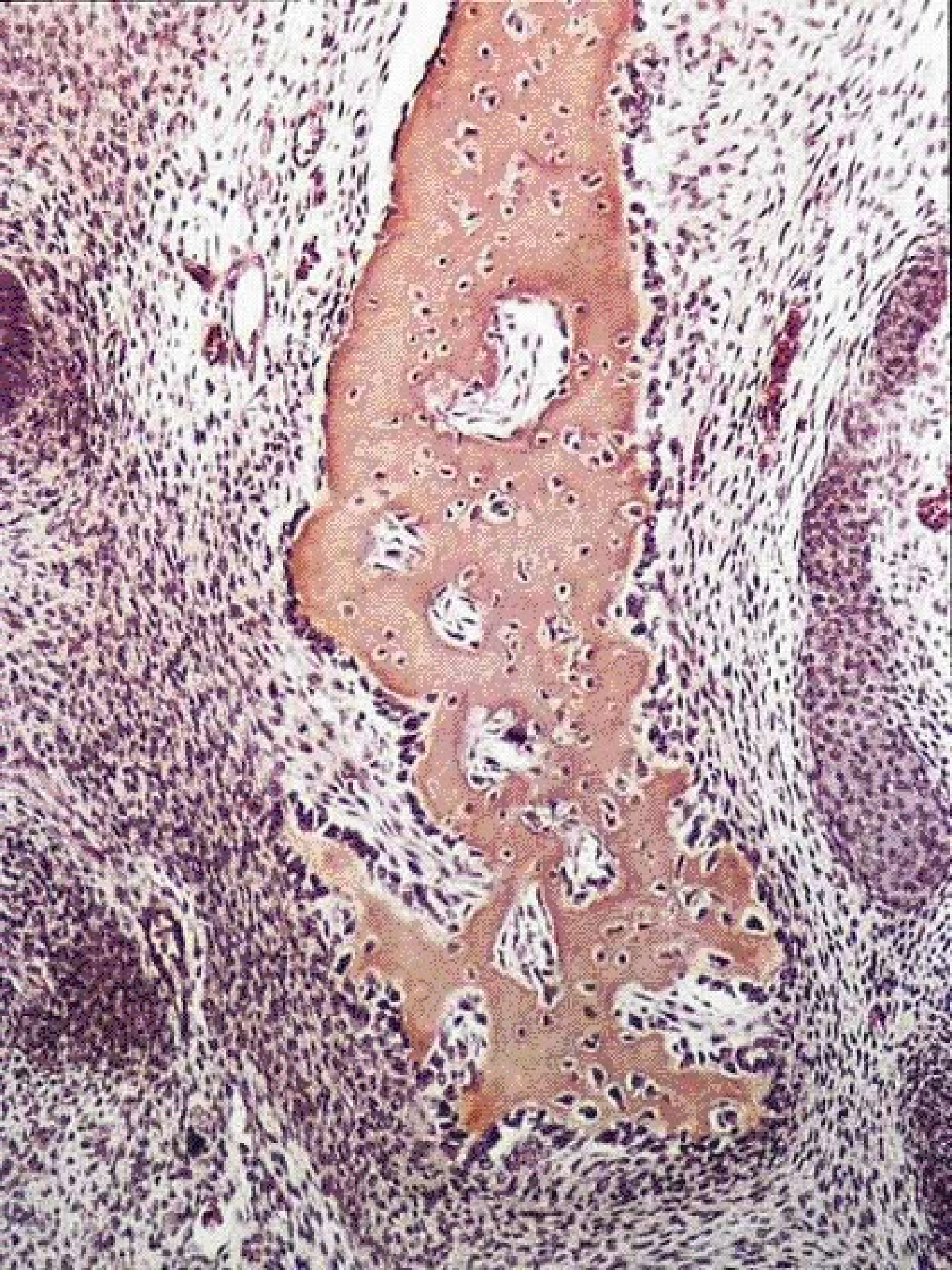


Step 2: As the spicules interconnect, they trap blood vessels within the bone. (LM× 23)



Step 3: Over time, the bone assumes the structure of spongy bone. Areas of spongy bone may later be removed, creating marrow cavities. Through remodeling, spongy bone formed in this way can be converted to compact bone.





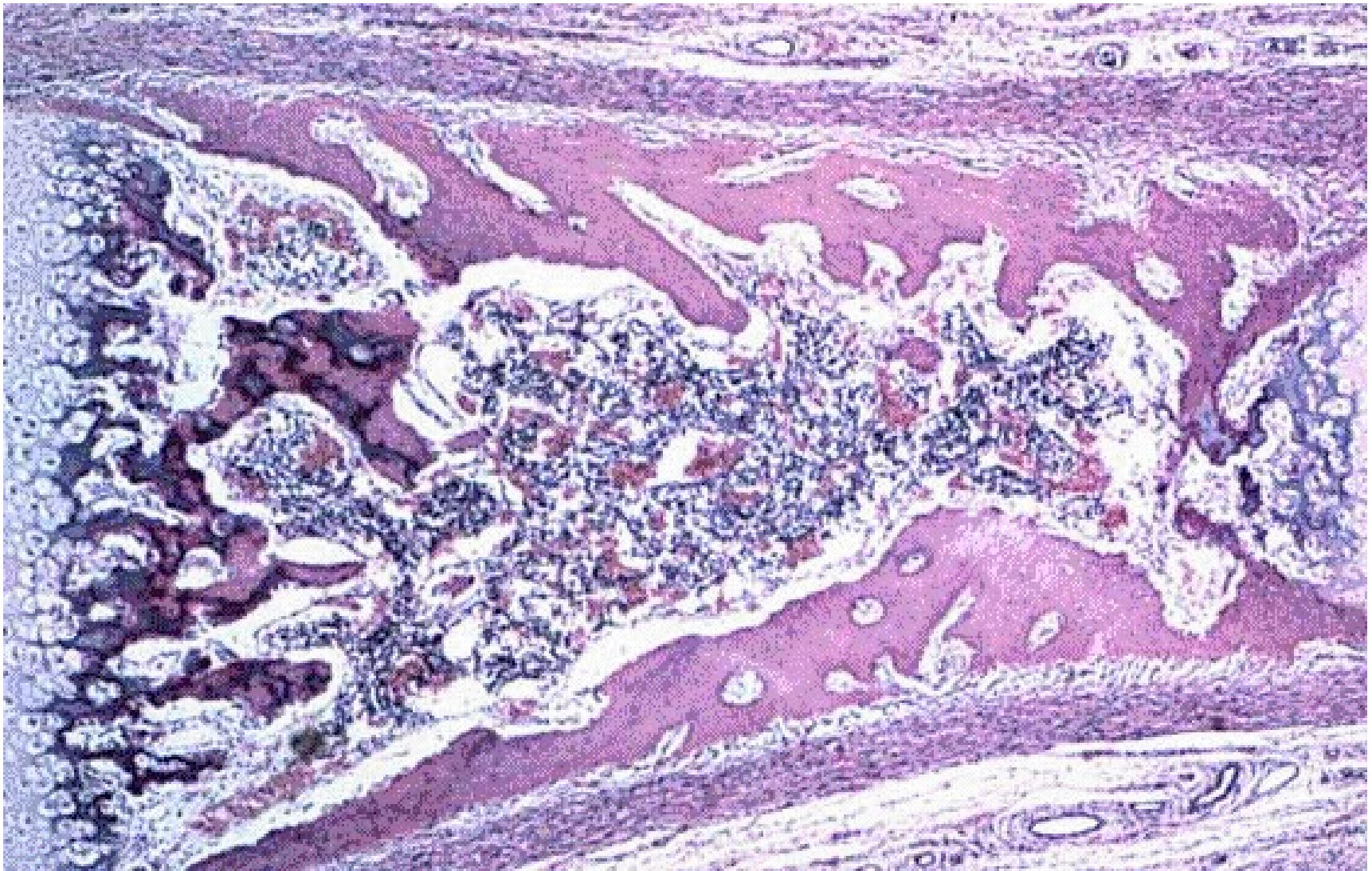
BONE FORMATION

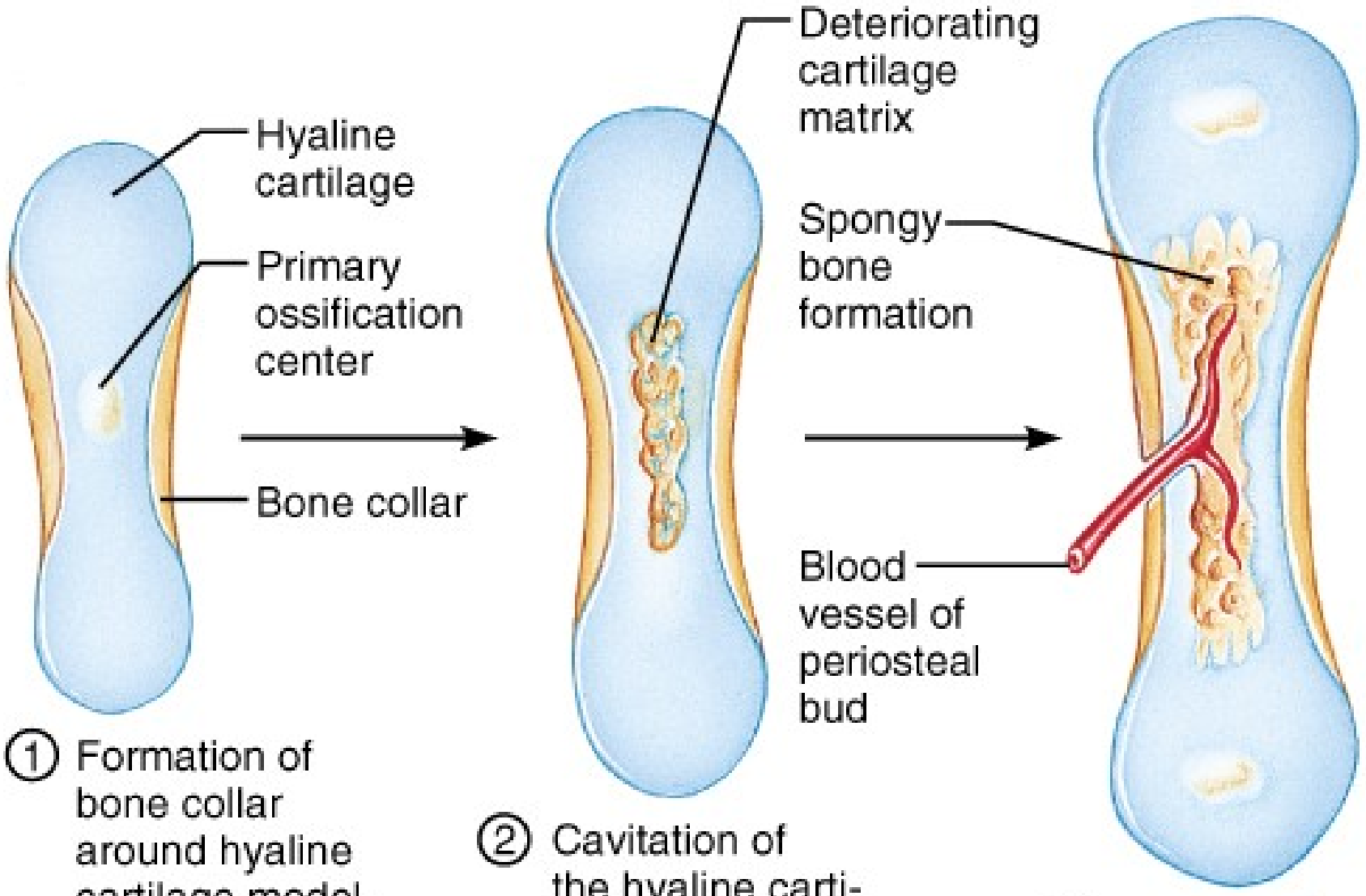
- **Endochondral ossification**
  - Uses a hyaline cartilage model
  - Dead cartilage cells become vascularized => osteoblasts

LONG BONE FORMATION

- Compact bone
  - "Collar" forms at nutrient aa
- Primary center
  - Middle of diaphysis
- Secondary centers
  - Each epiphysis
- Cartilage remnants

ENDOCHONDRAL OSSIFICATION

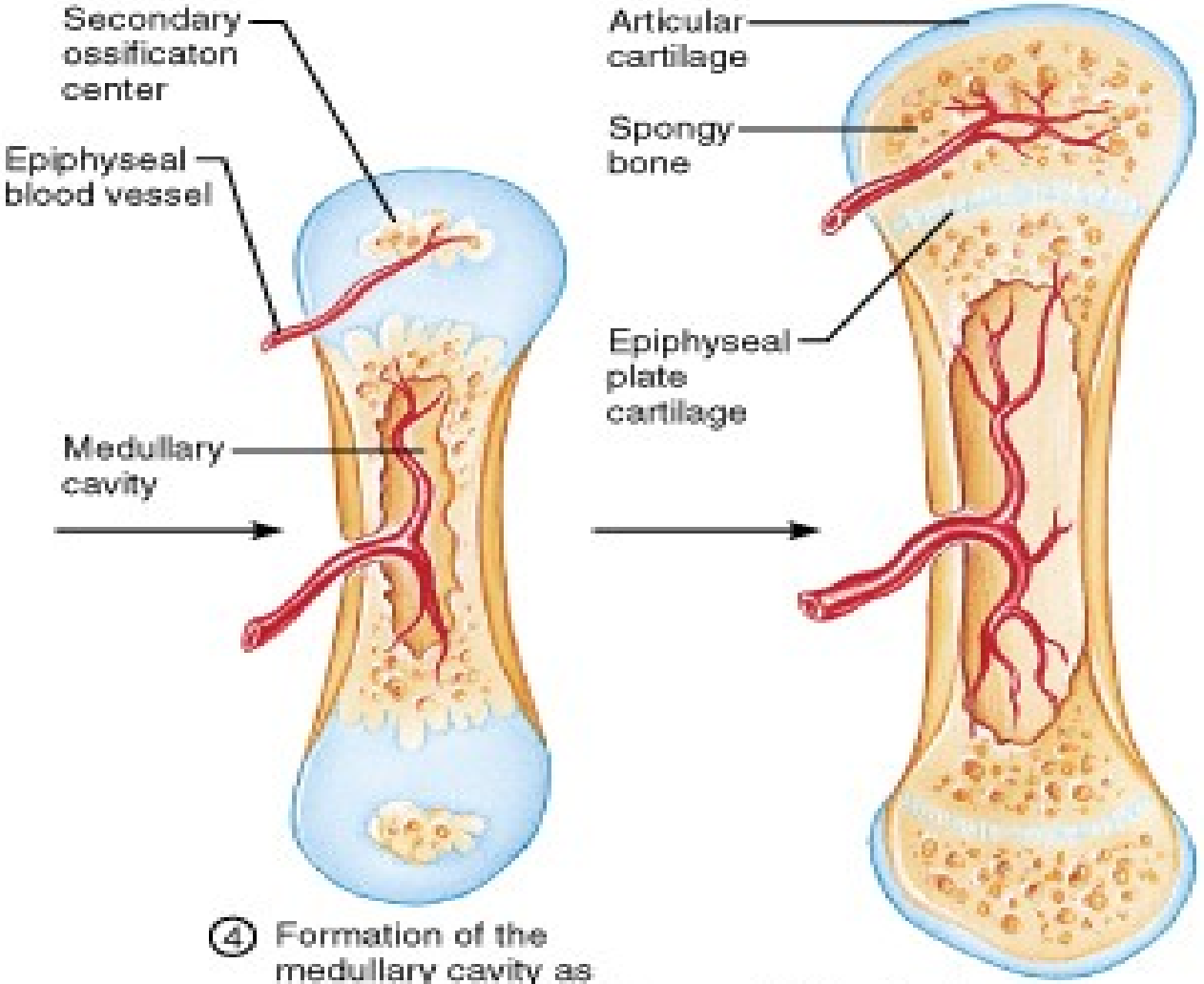




① Formation of bone collar around hyaline cartilage model.

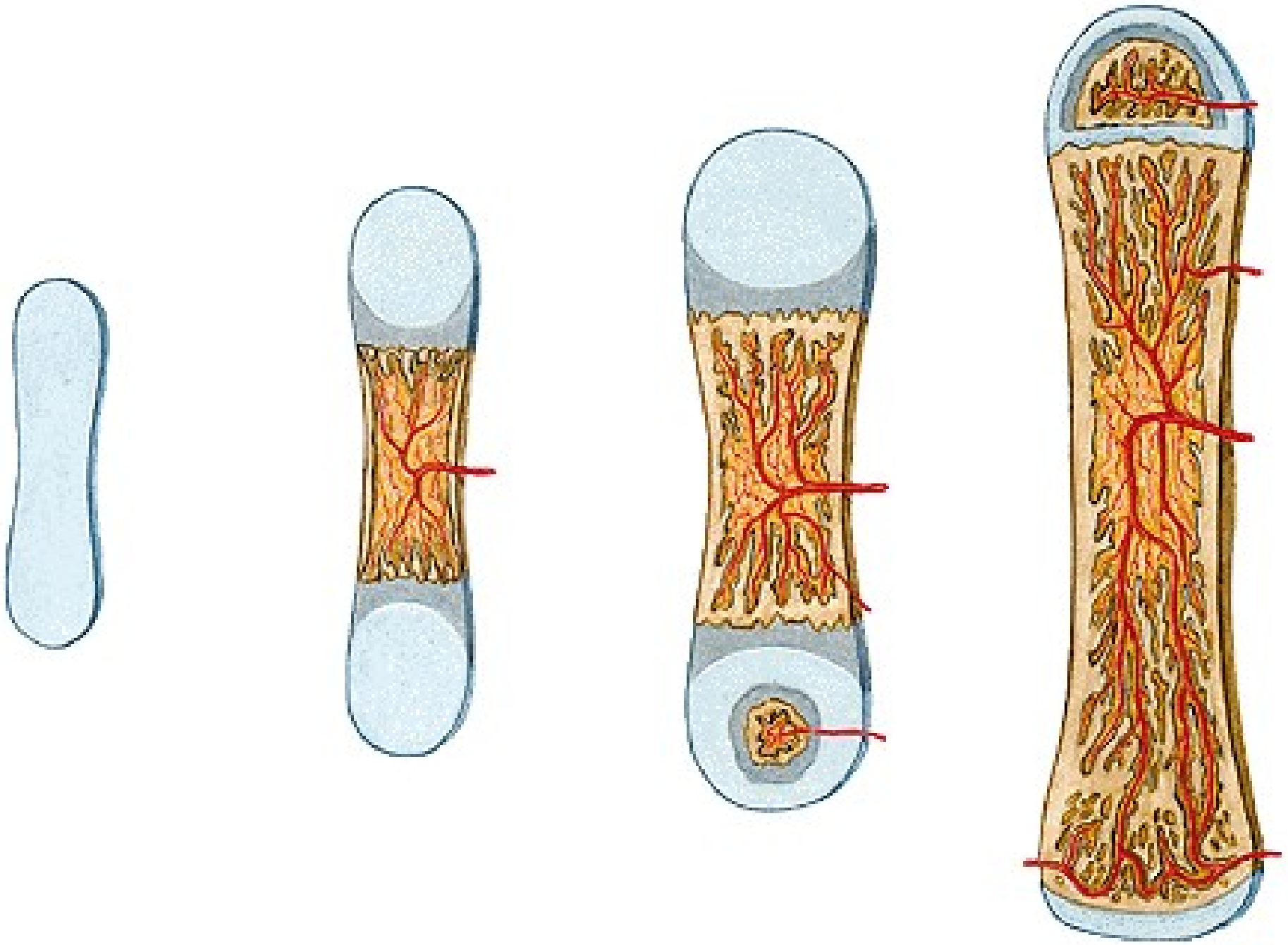
② Cavitation of the hyaline cartilage within the cartilage model.

③ Invasion of internal cavities by the periosteal bud and spongy bone formation.



④ Formation of the medullary cavity as ossification continues; appearance of secondary ossification centers in the epiphyses in preparation for stage 5.

⑤ Ossification of the epiphyses; when completed, hyaline cartilage remains only in the epiphyseal plates and articular cartilages. (The epiphyseal plates promote longitudinal growth until young adulthood.)



BONE GROWTH

- Similar to cartilaginous growth
  - ***Appositional*** (thickness)
  - ***Interstitial*** (length)
- **Hyaline**, type II collagen

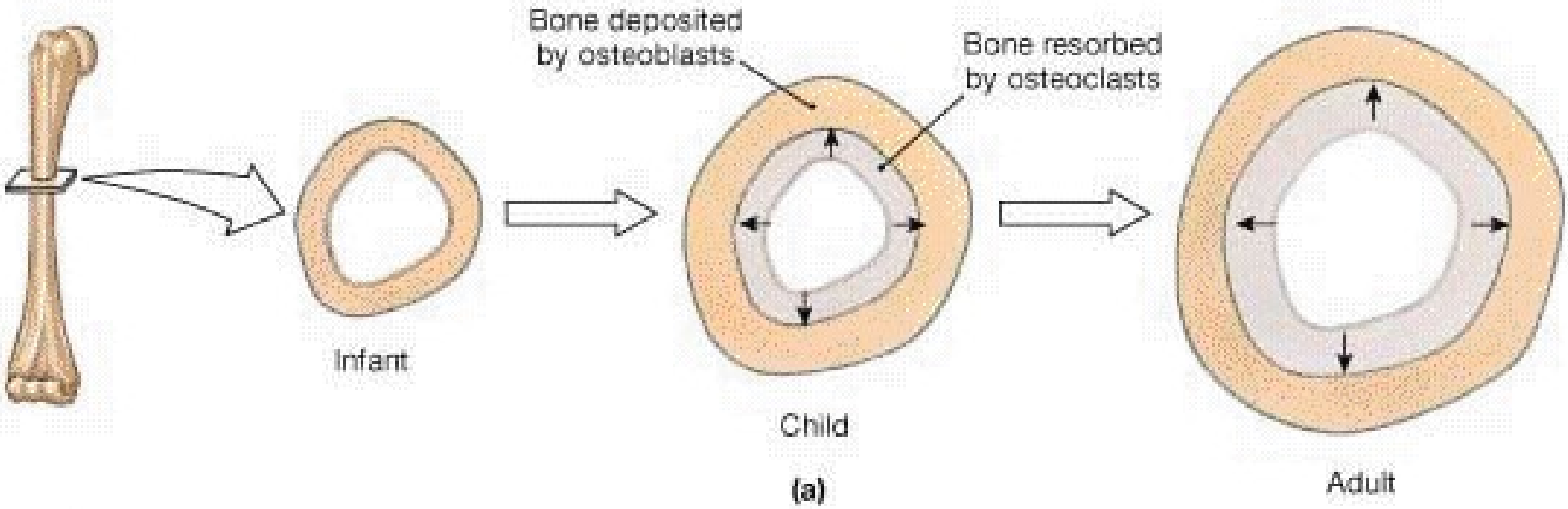
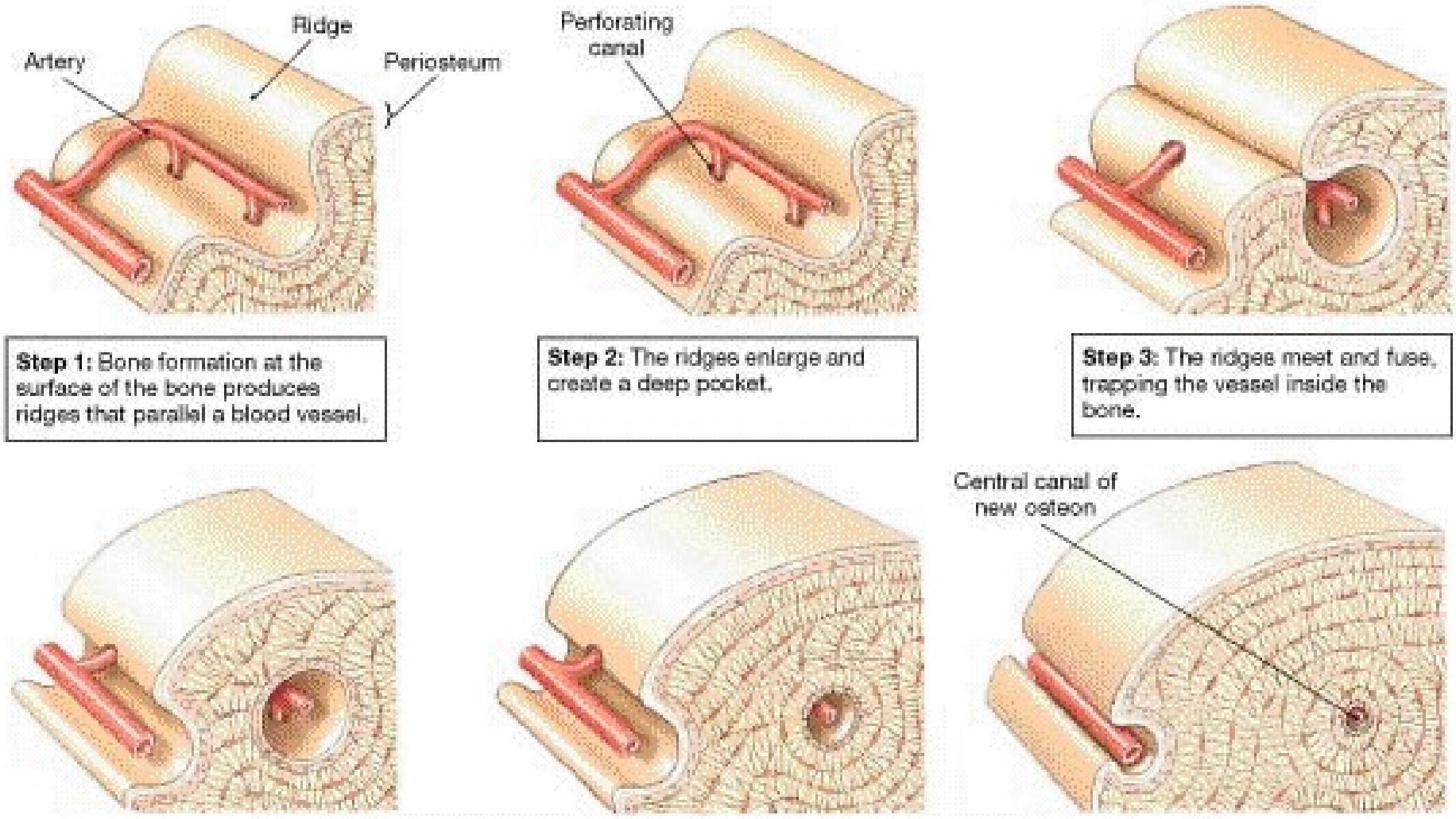


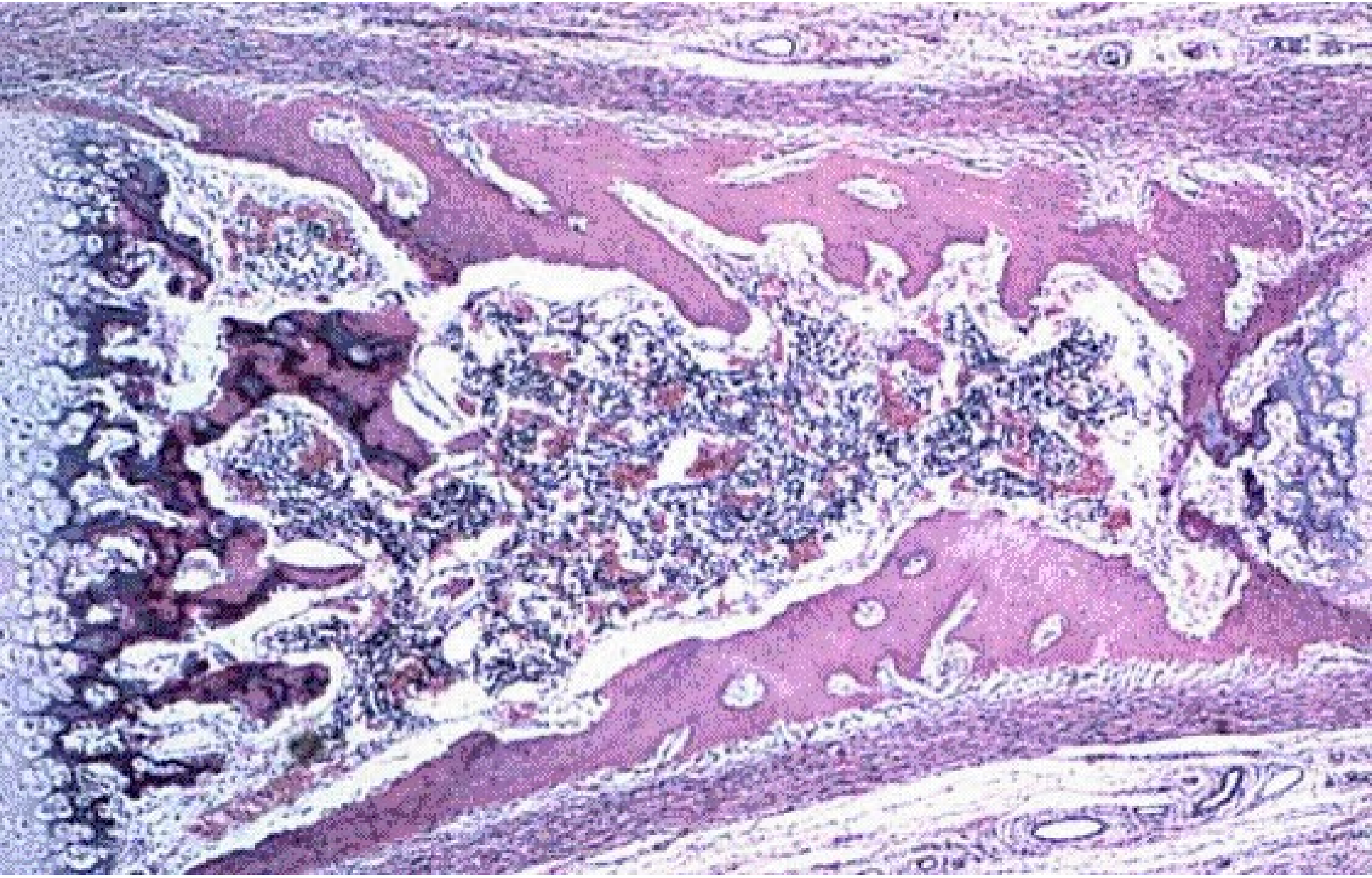
FIGURE 6-11 Appositional Bone Growth. **(a)** A bone grows in diameter as new bone is added to the outer surface. At the same time, osteoclasts resorb bone on the inside, enlarging the marrow cavity.

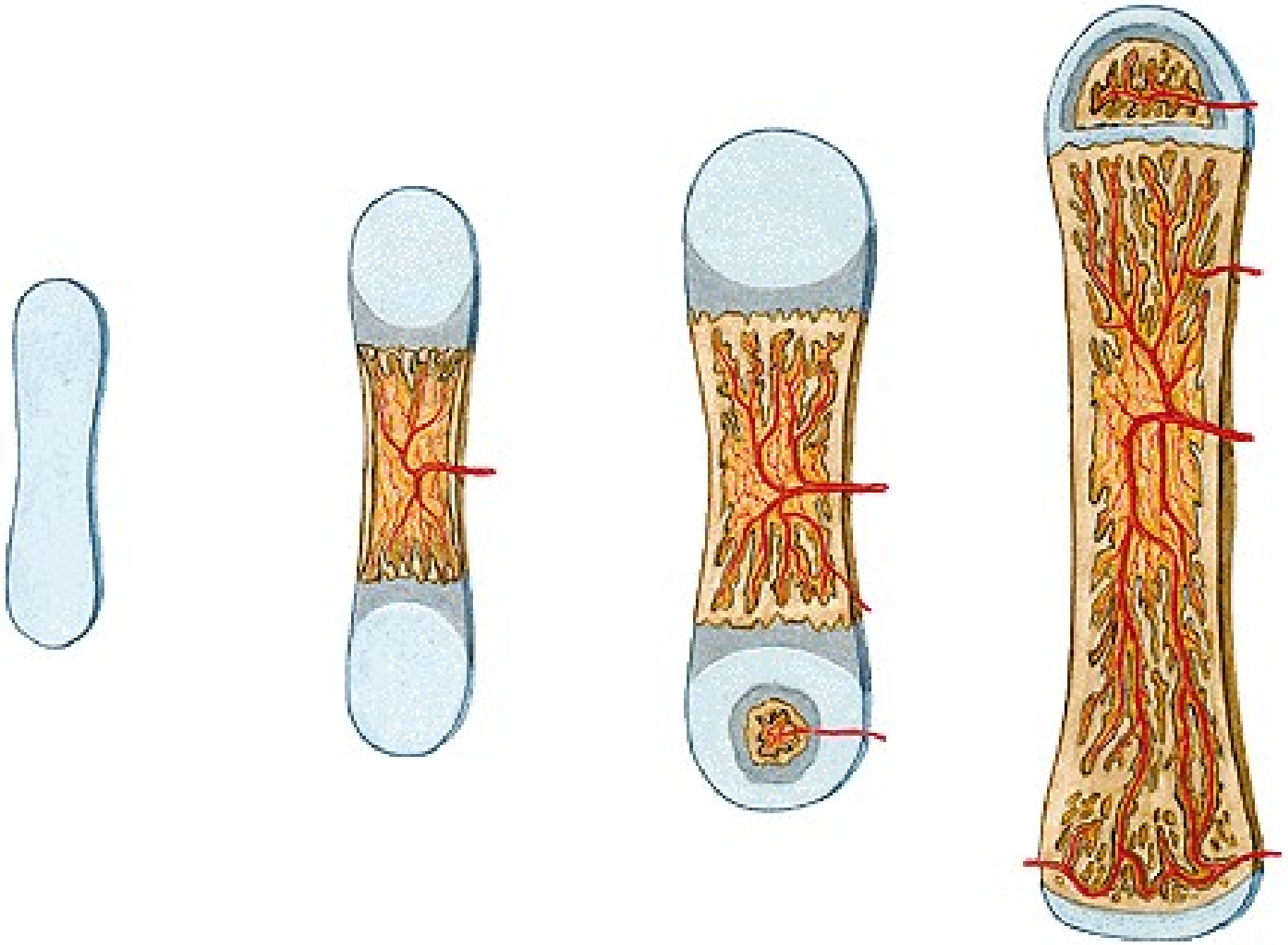


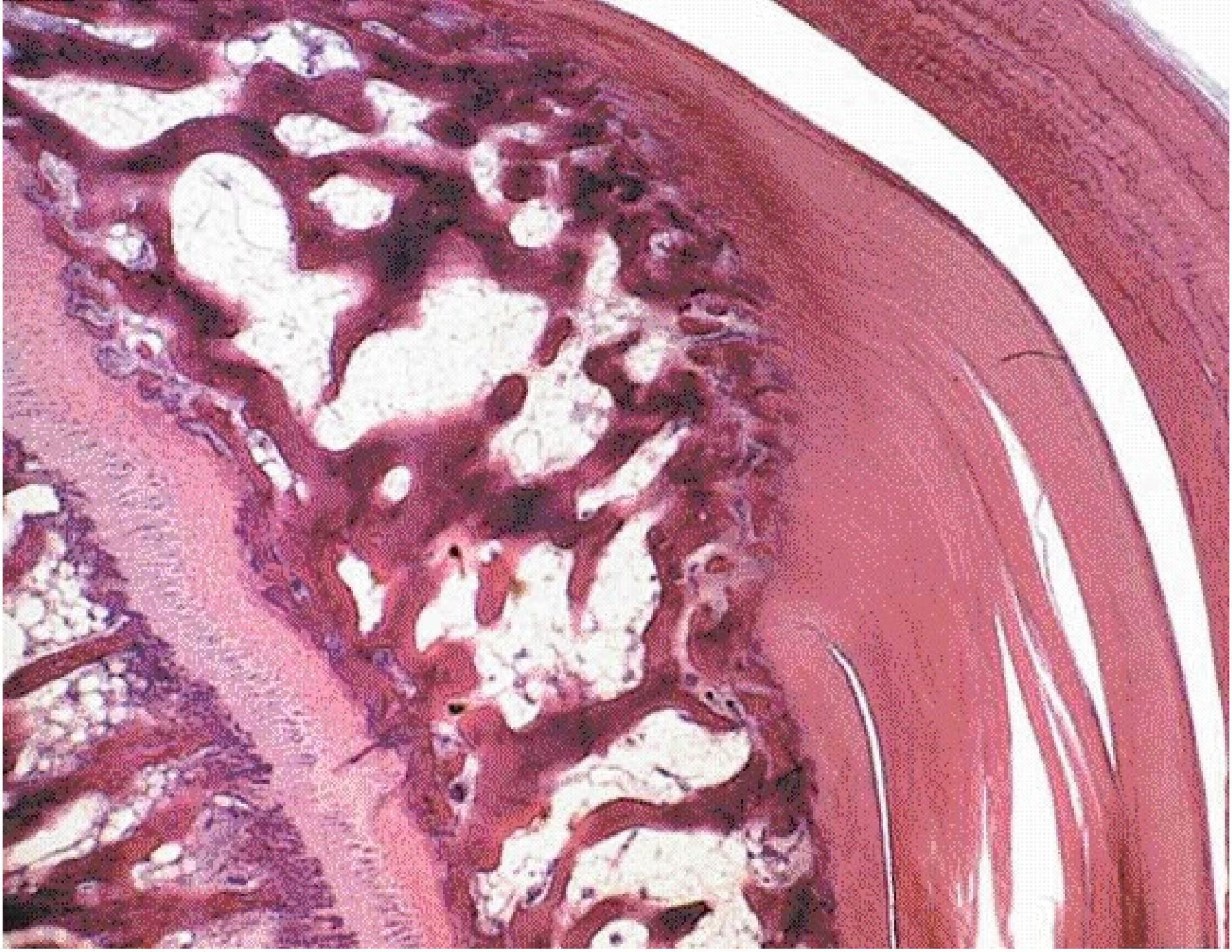
● ***FIGURE 6-11*** **Appositional Bone Growth.** **(b)** Three-dimensional diagrams illustrating the mechanism responsible for increasing the diameter of a growing bone.

INTERSTITIAL GROWTH

- Occurs at epiphyseal plate
- Forms “zones” of cartilage
  - Zone of resting cartilage
  - Zone of proliferating cartilage
  - Zone of hypertrophy
  - Zone of calcified cartilage







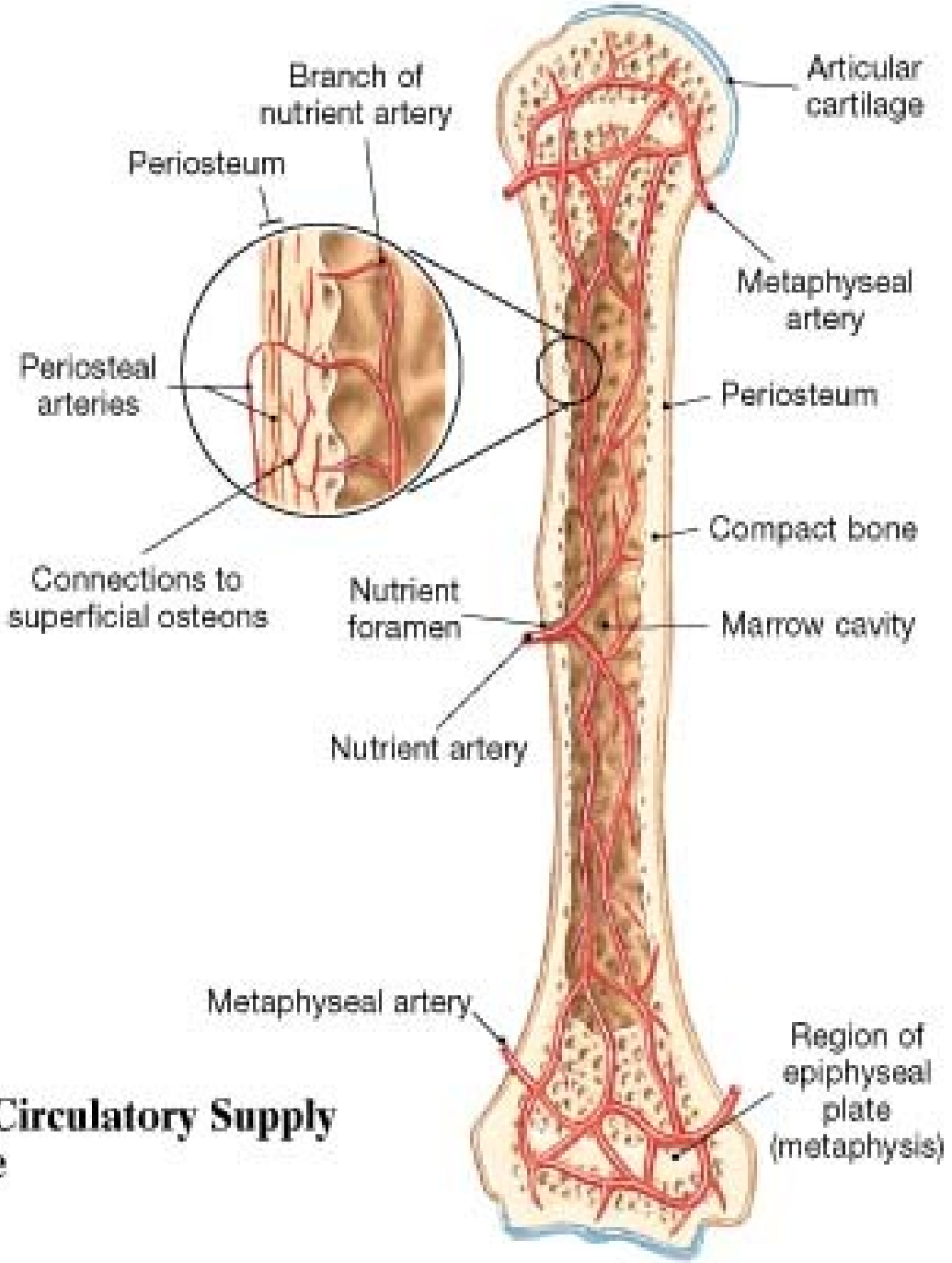


FIGURE 6-12 Circulatory Supply to a Mature Bone

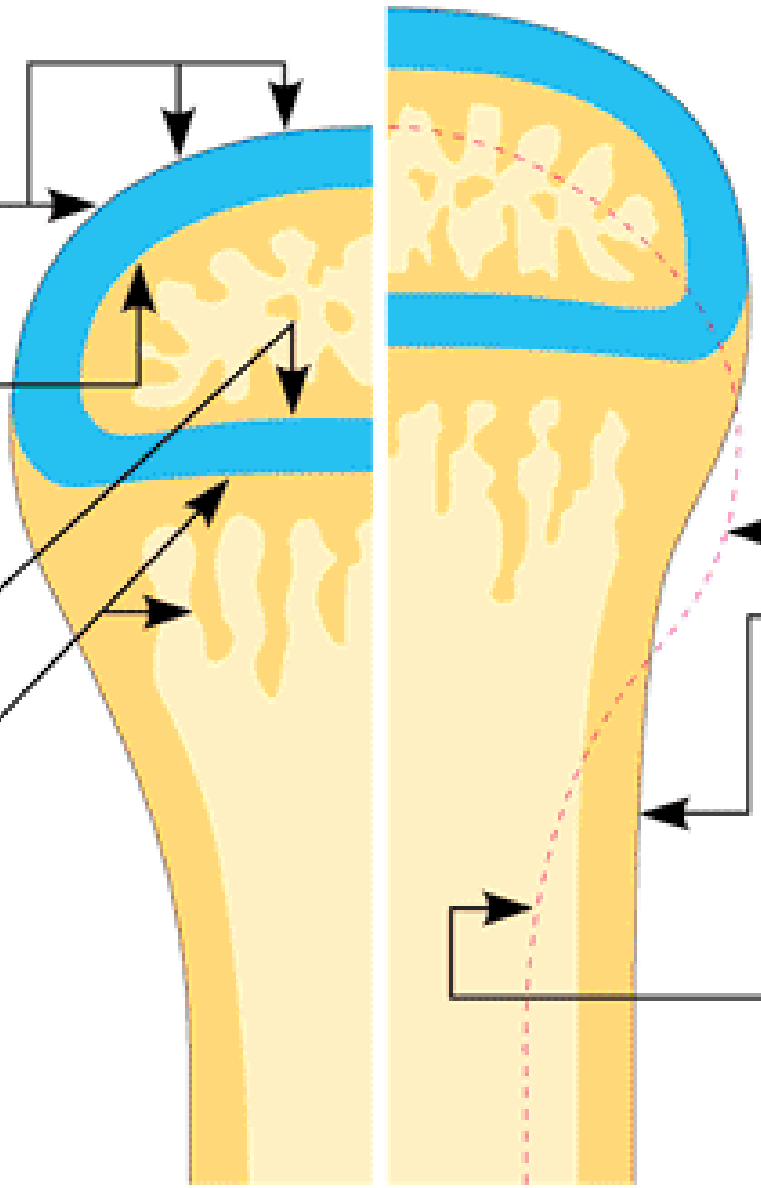
BONE REMODELING

- Osteoclast digest old bone
- Reshaped throughout growth
- Osteoblast reinforce weak areas
- Ground substance turnover
  - Stress: stimulates new bone
  - Lack of stress: “space”
    - Osteoclast reabsorb bone

Growth

Bone grows in length because:

1. Cartilage grows here
2. Cartilage replaced by bone here
3. Cartilage grows here
4. Cartilage replaced by bone here



Remodeling

Growing shaft is remodeled by:

1. Bone resorbed here
2. Bone added by appositional growth here
3. Bone resorbed here

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BONE HOMEOSTASIS

- Minerals
- Vitamins
- Hormones
- Effects of Aging

HORMONAL REGULATION

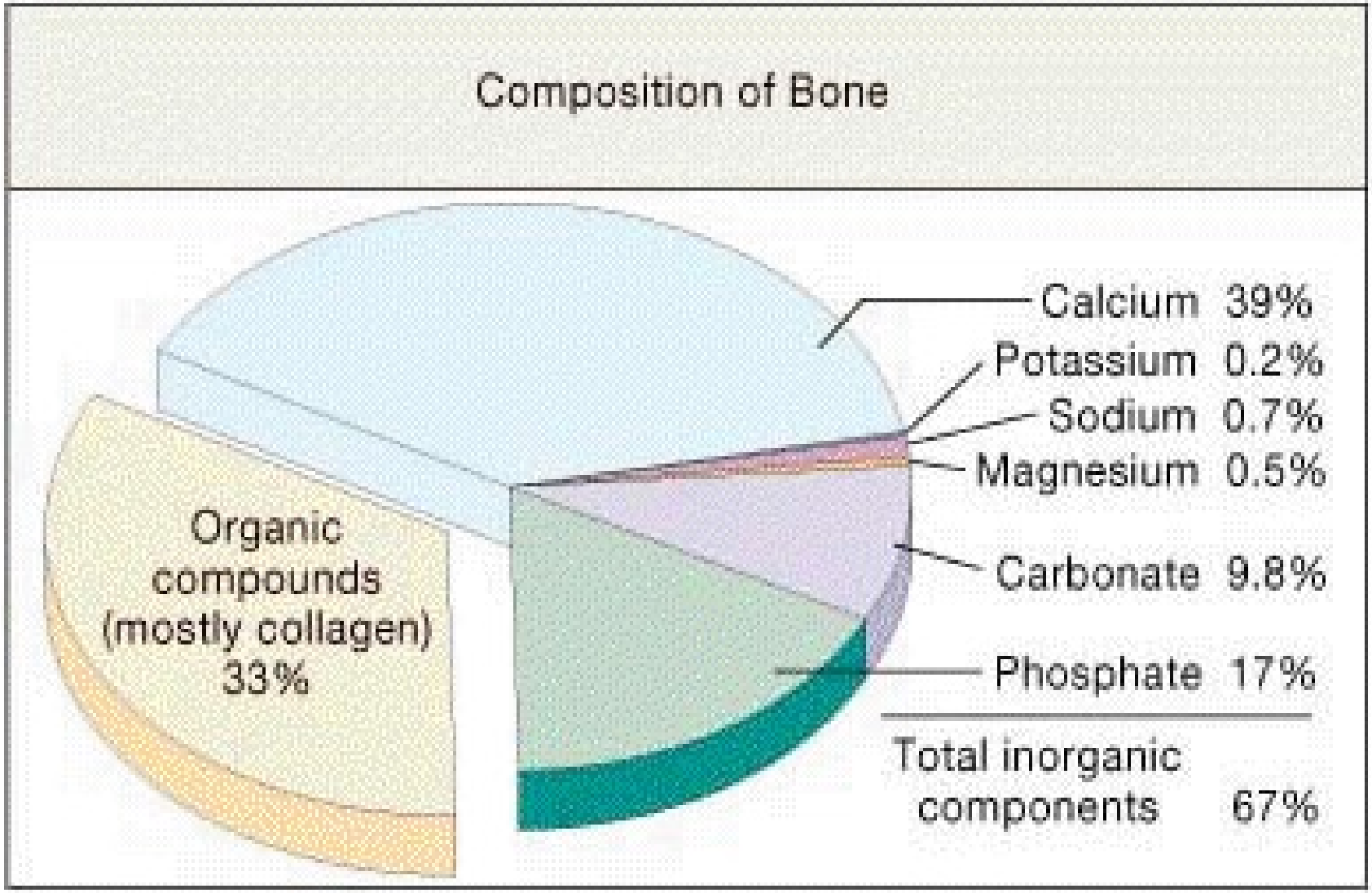
- Prepuberty
  - Human growth hormone (hGH)
  - Insulin-like growth factors
  - Thyroid hormones
  - Insulin from pancreas

HORMONAL REGULATION

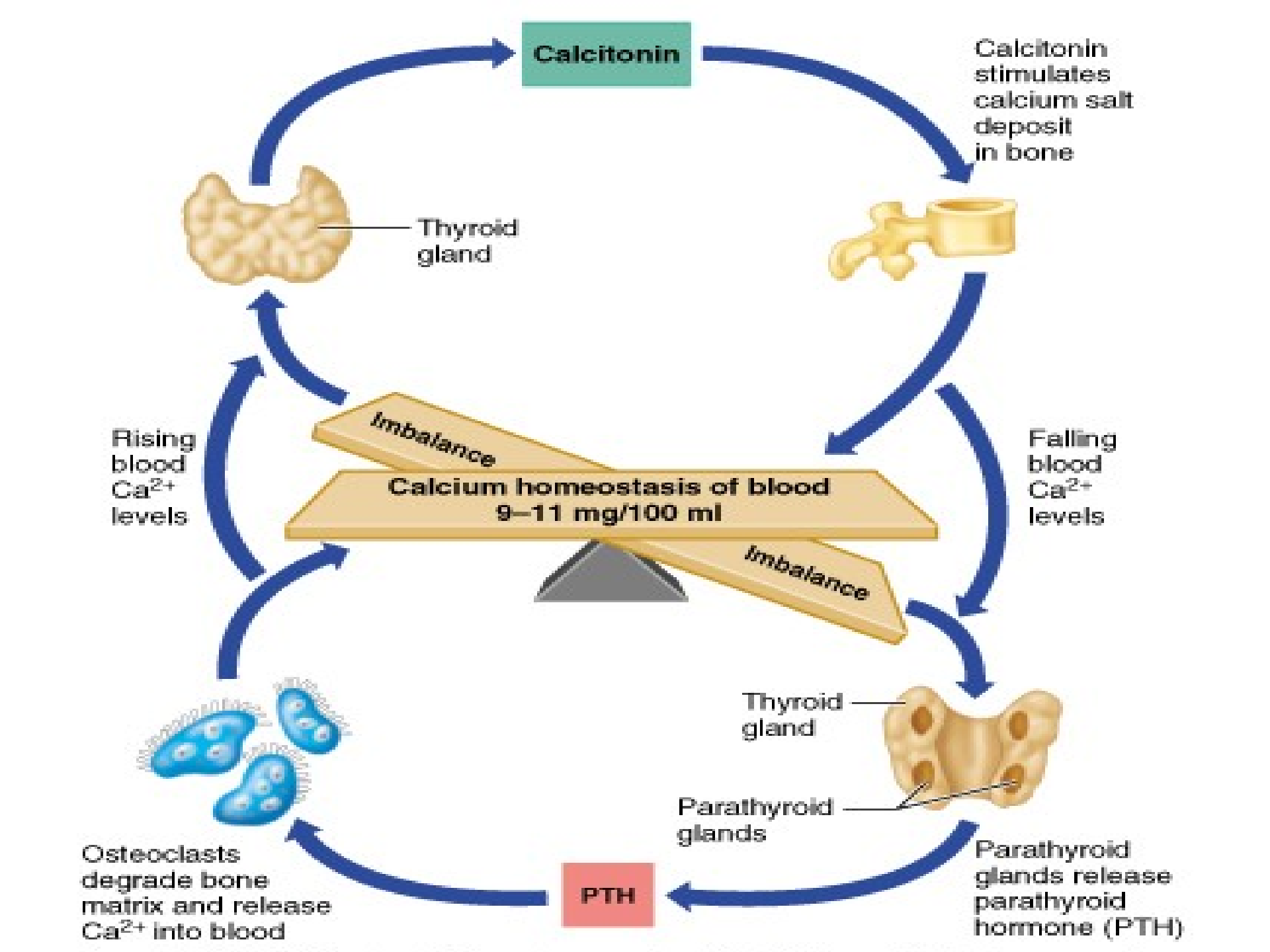
- At puberty
  - Sex hormones => growth spurt
    - **Estrogen**: females
    - **Testosterone**: males

BONE MAKE-UP

- Site of mineral reserve



A Chemical Analysis of Bone

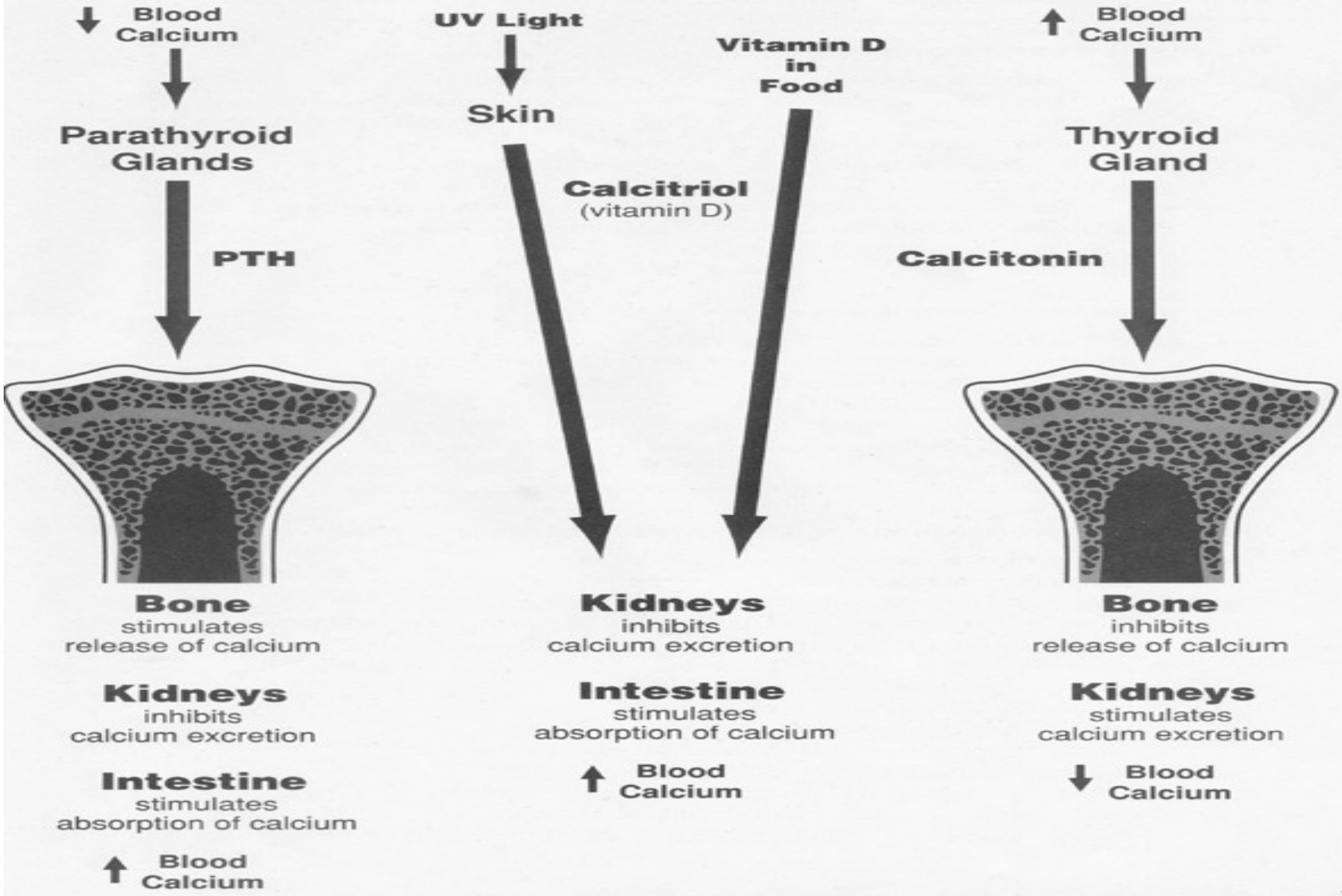

Calcitonin
Calcitonin stimulates calcium salt deposit in bone
Thyroid gland
Rising blood Ca^{2+} levels
Imbalance
Calcium homeostasis of blood
9–11 mg/100 ml
Imbalance
Falling blood Ca^{2+} levels
Thyroid gland
Parathyroid glands
Osteoclasts degrade bone matrix and release Ca^{2+} into blood
PTH
Parathyroid glands release parathyroid hormone (PTH)

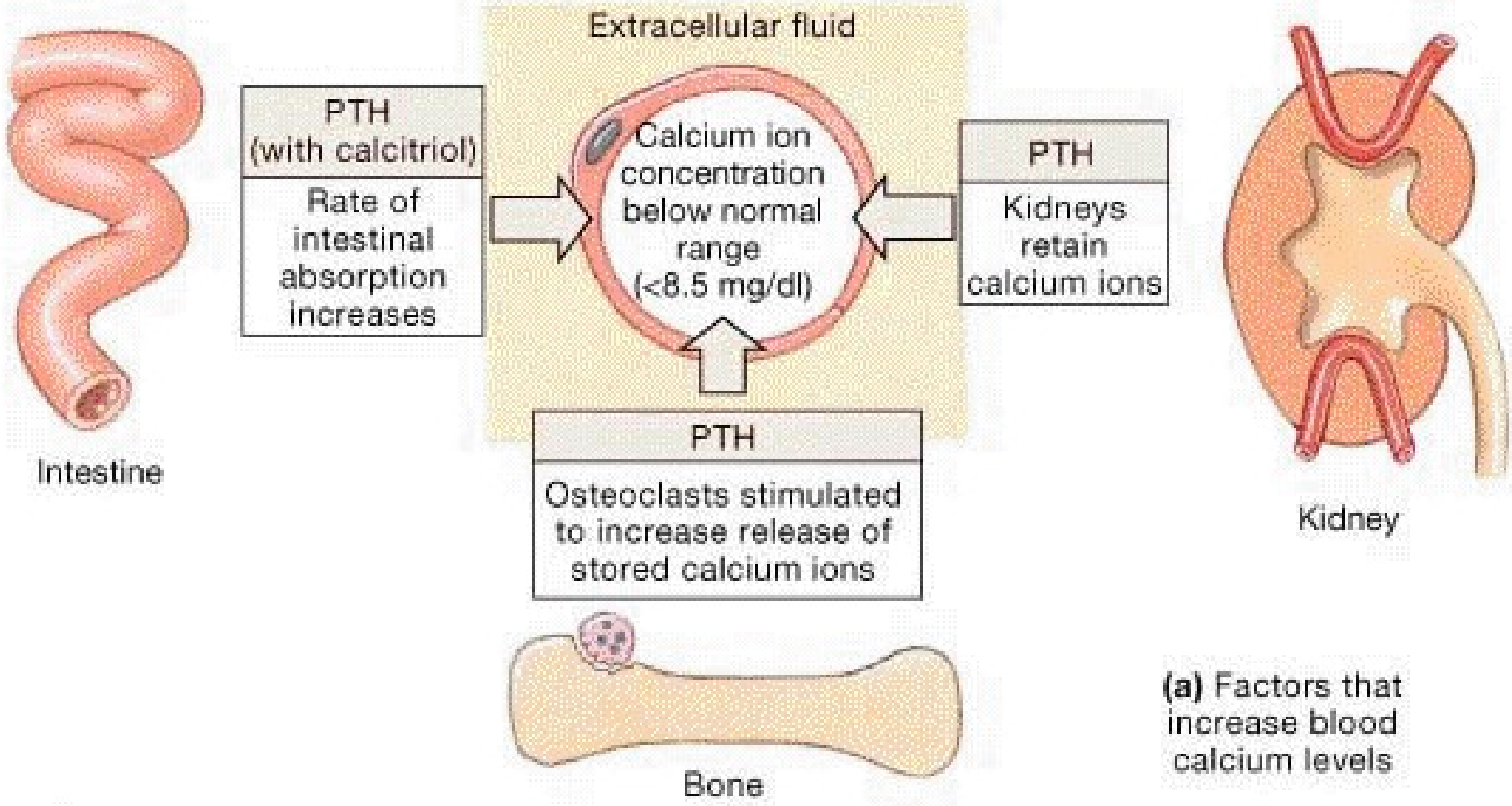
CALCIUM "HOMEOSTASIS"

- VERY NARROW range of normal
  - 30% increase - nerve/muscle cells fail
  - 35% decrease - body convulses
  - 50% decrease - death
- Rarely changes by more than 10%

CALCIUM BALANCE

Calcium homeostasis is regulated by Parathyroid Hormone (PTH), Calcitriol, and Calcitonin





• ***FIGURE 6-14*** **Factors That Alter the Concentration of Calcium Ions in Body Fluids.** **(a)** Factors that increase blood calcium ion concentrations.

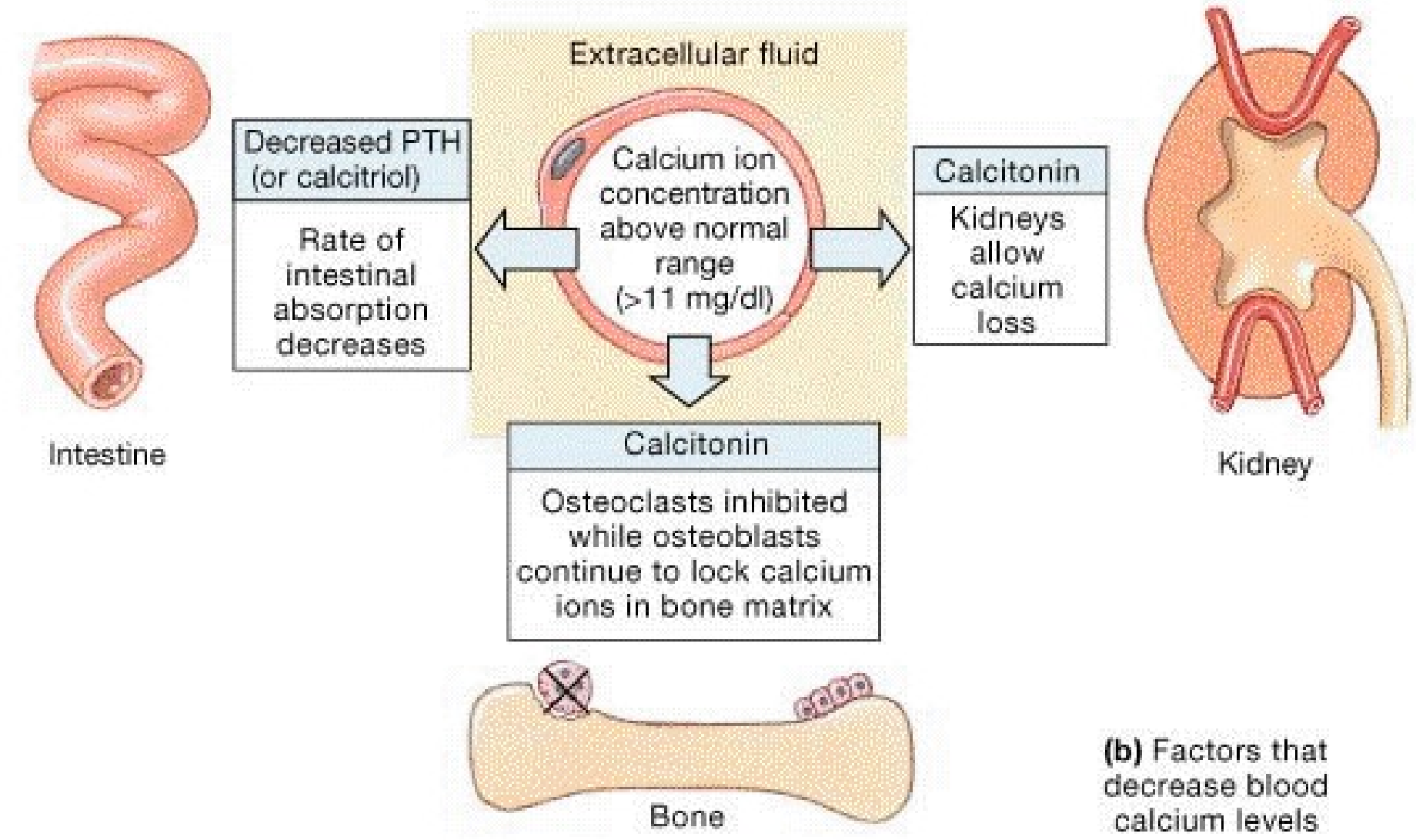
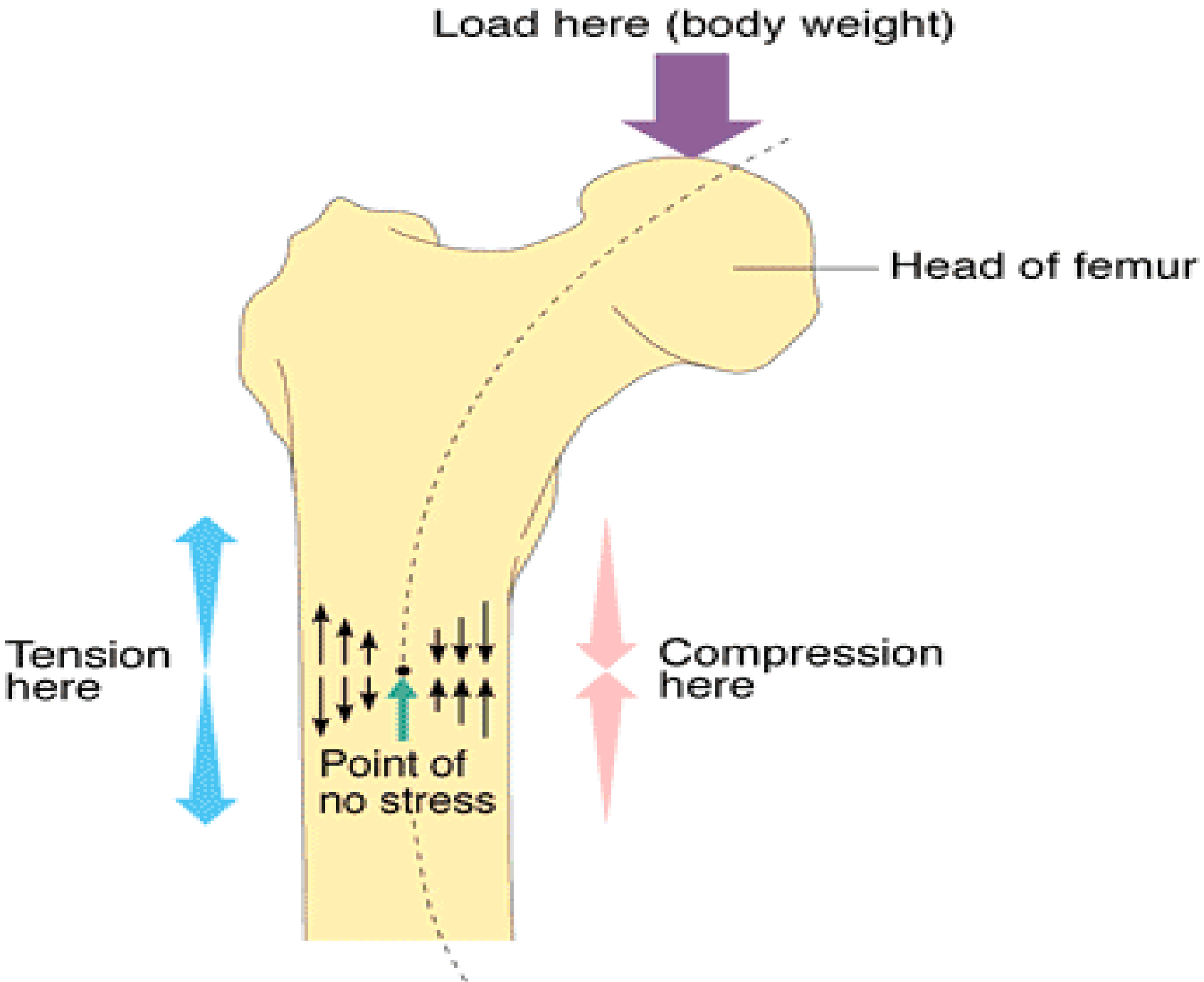
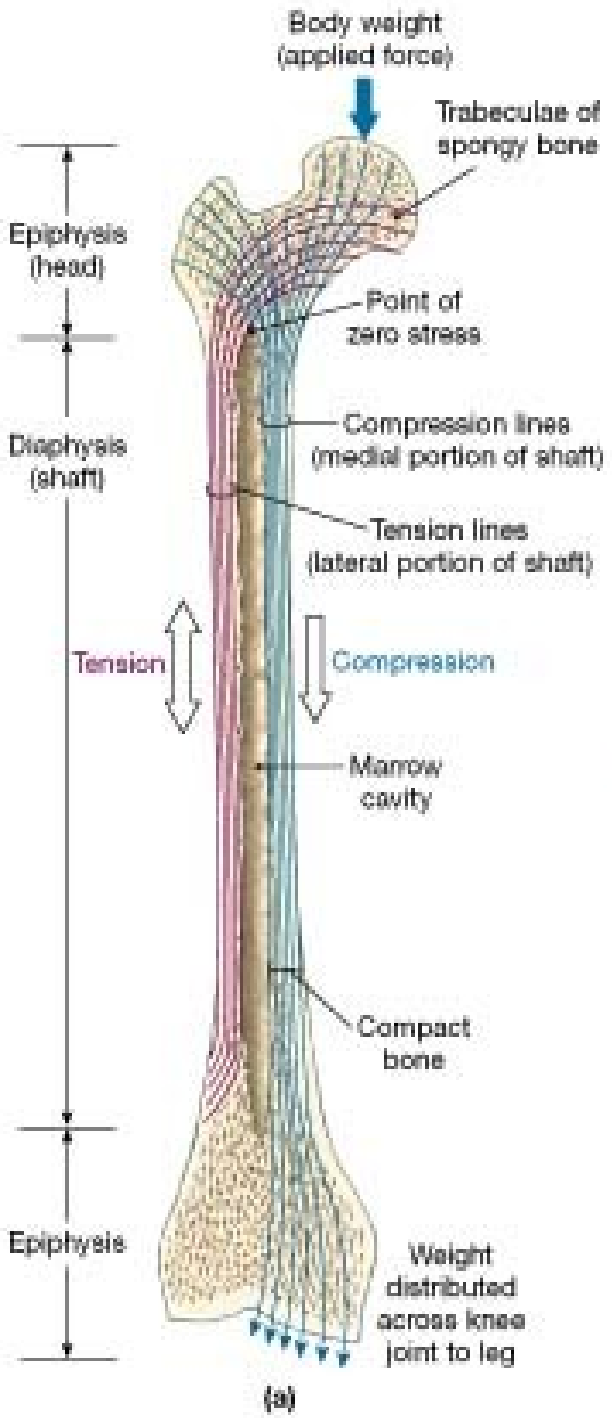
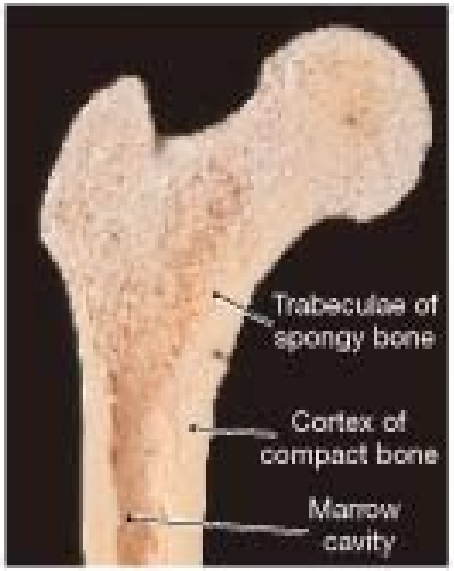


FIGURE 6-14 Factors That Alter the Concentration of Calcium Ions in Body Fluids.
(b) Factors that decrease blood calcium ion concentrations.


Load here (body weight)
Head of femur
Tension here
Compression here
Point of no stress





(b)

FIGURE 6-5 Lamellar Organization in a Long Bone. **(a)** The femur, or thigh bone, has a diaphysis (shaft) with walls of compact bone and epiphyses (heads) filled with spongy bone. The body weight is transferred to the femur at the hip joint. Because the hip joint is off-center relative to the axis of the shaft, the body weight is distributed along the bone such that the medial (inner) portion of the shaft is compressed and the lateral (outer) portion is stretched. **(b)** A photograph showing the epiphysis after sectioning. Compare the orientation of trabeculae with the stress lines indicated in (a).

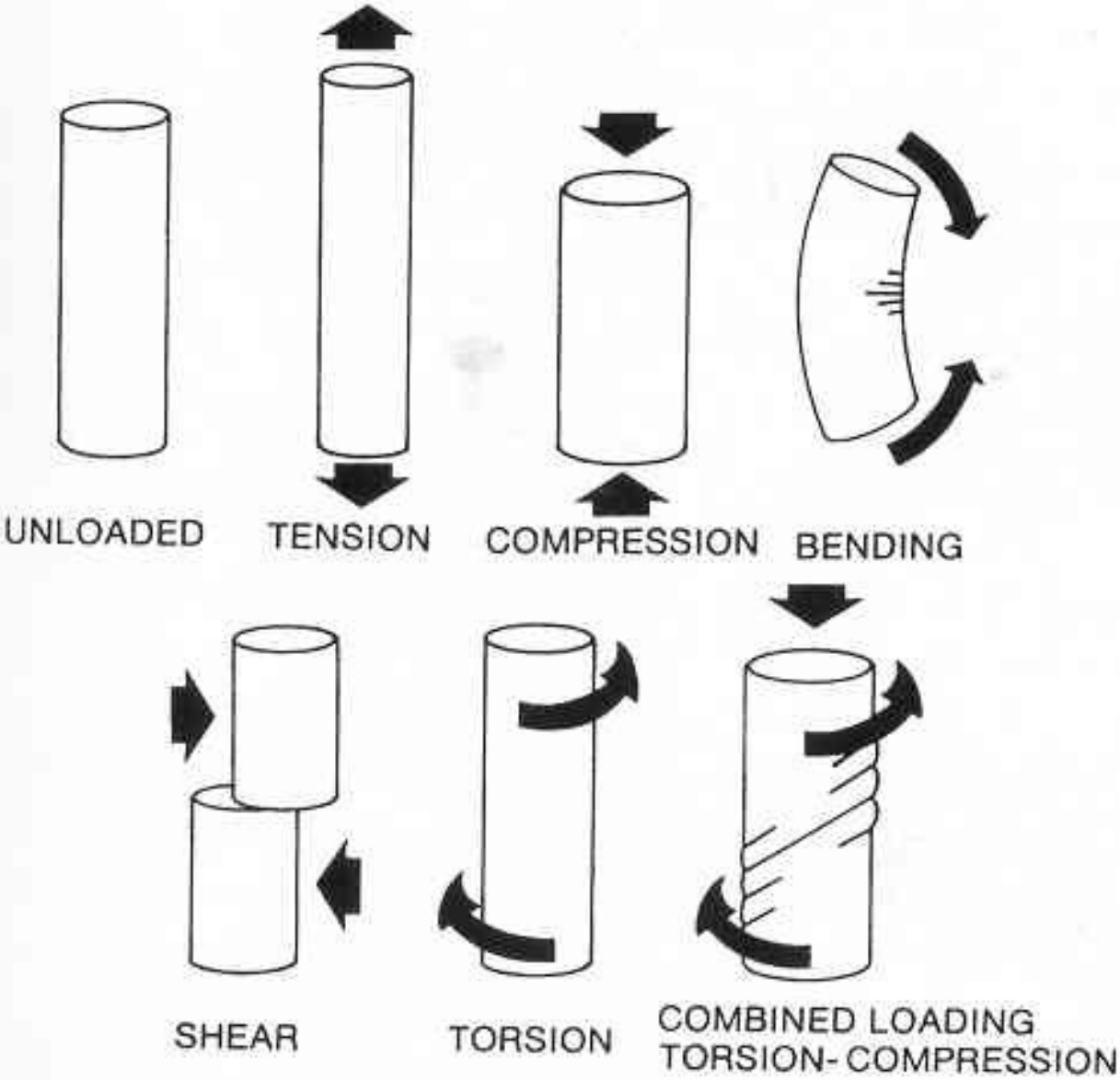


Figure 6.1. Loading modes that affect long bones. (From Nordin & Frankel, 1980; reproduced with permission of authors and Williams & Wilkins.)

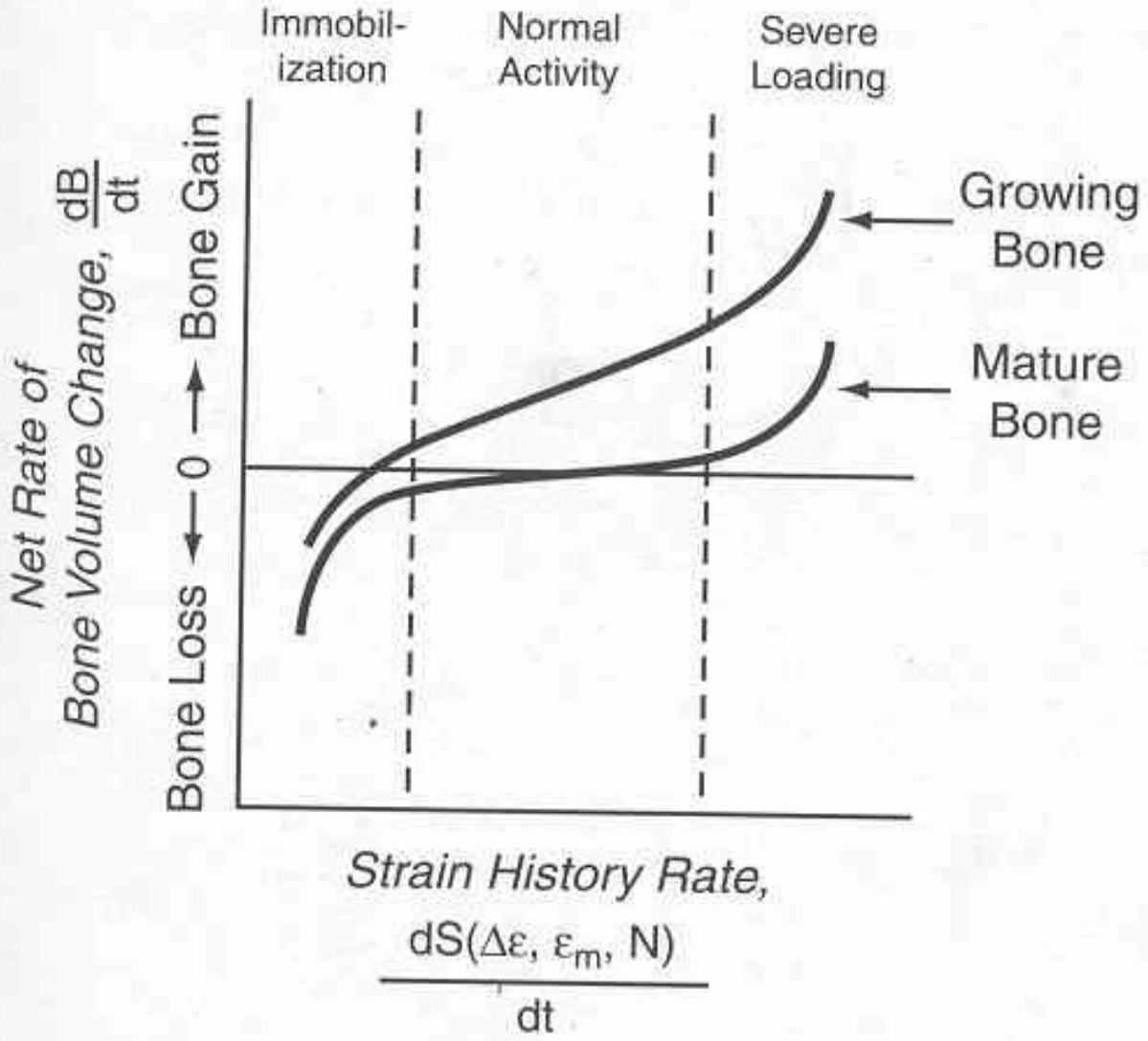
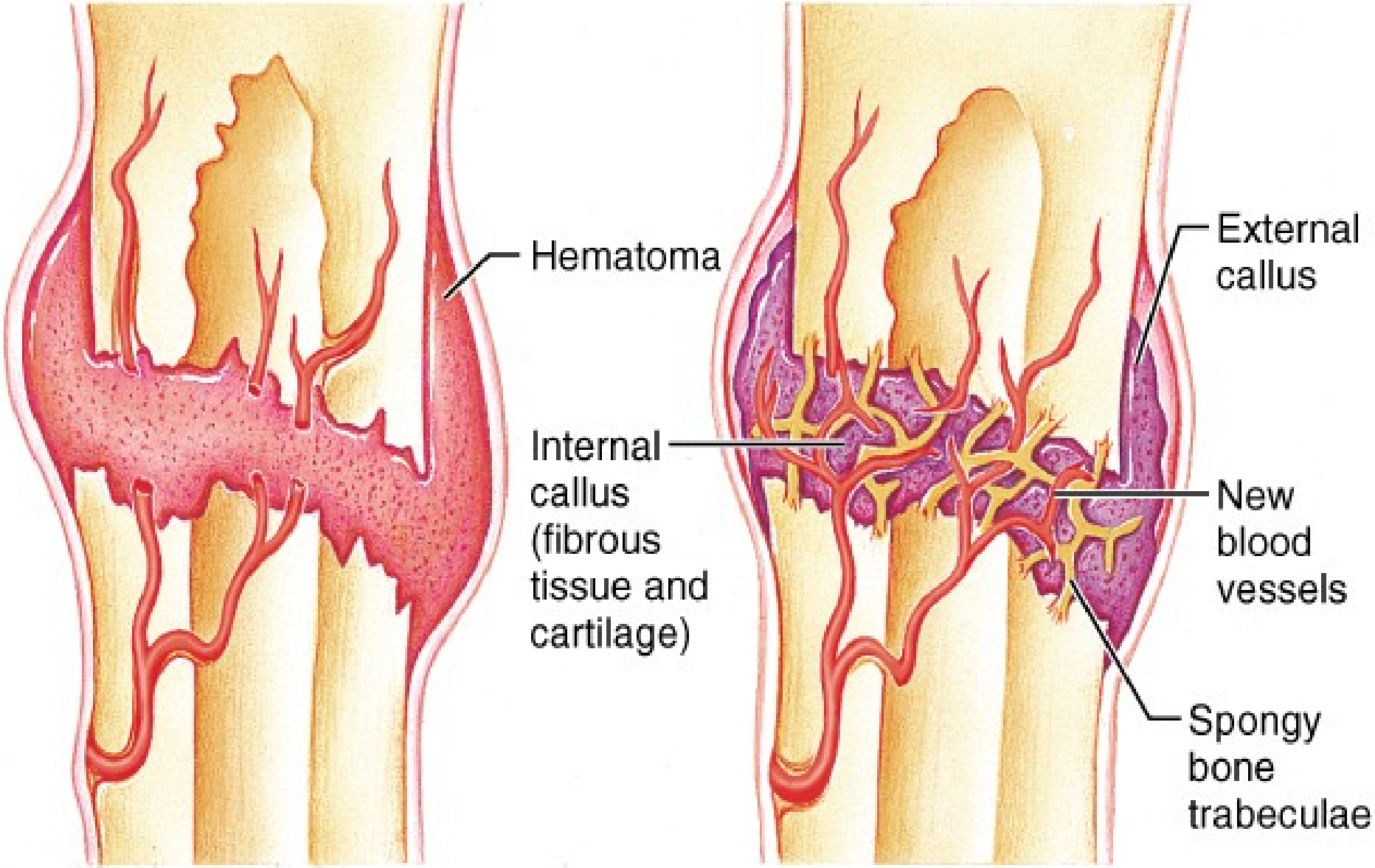


Figure 4.5. Hypothesis on the relationship between bone strain history and the net change in bone volume for mature and growing animals (from Carter, 1982).

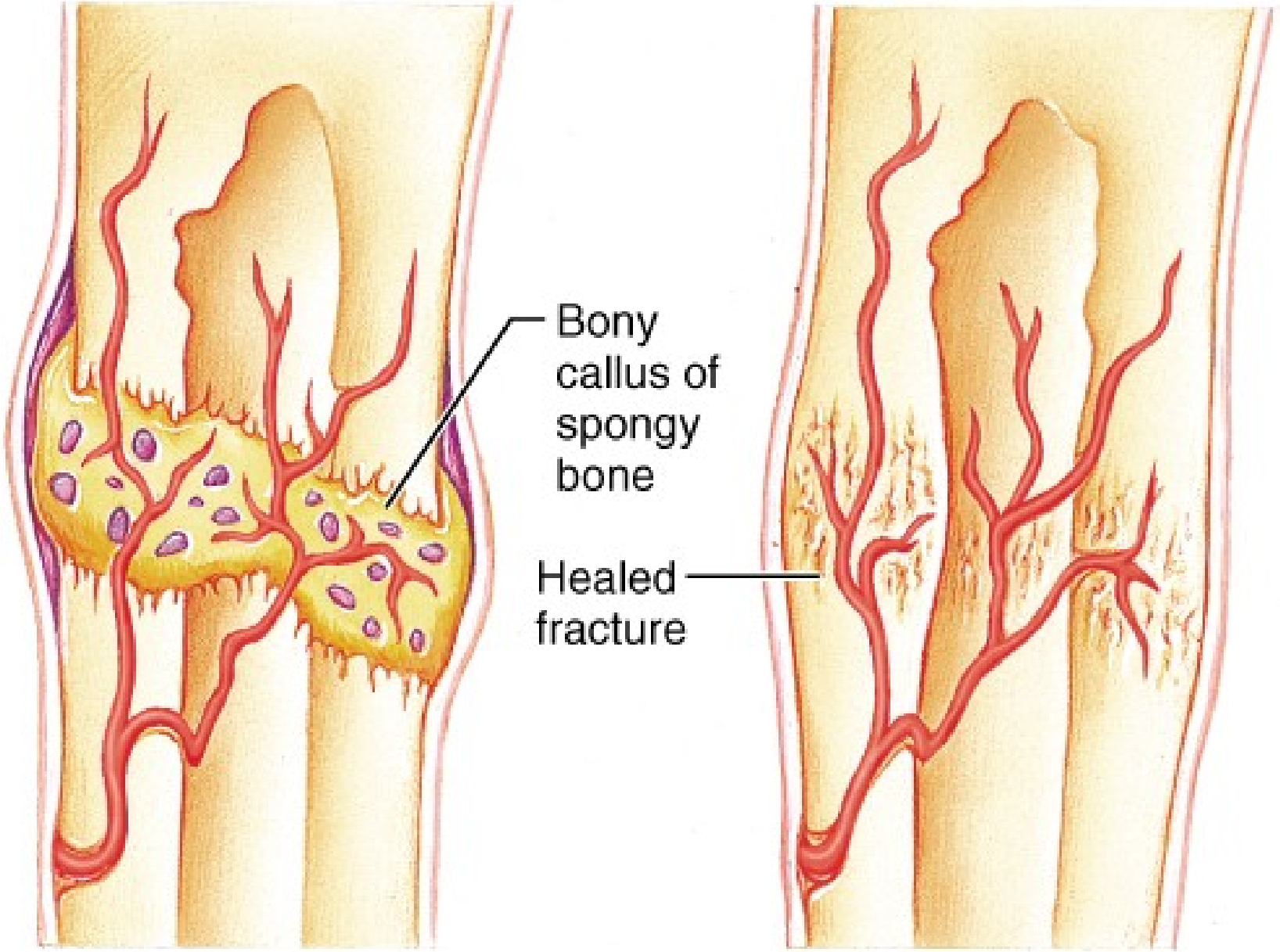
BONE REPAIR

- Four step process
  - Fracture hematoma forms
  - Callus formation
    - Internal callus (endosteum)
    - External callus (periosteum)
  - Spongy bone from cartilage
  - Remodeling



① **Hematoma formation**

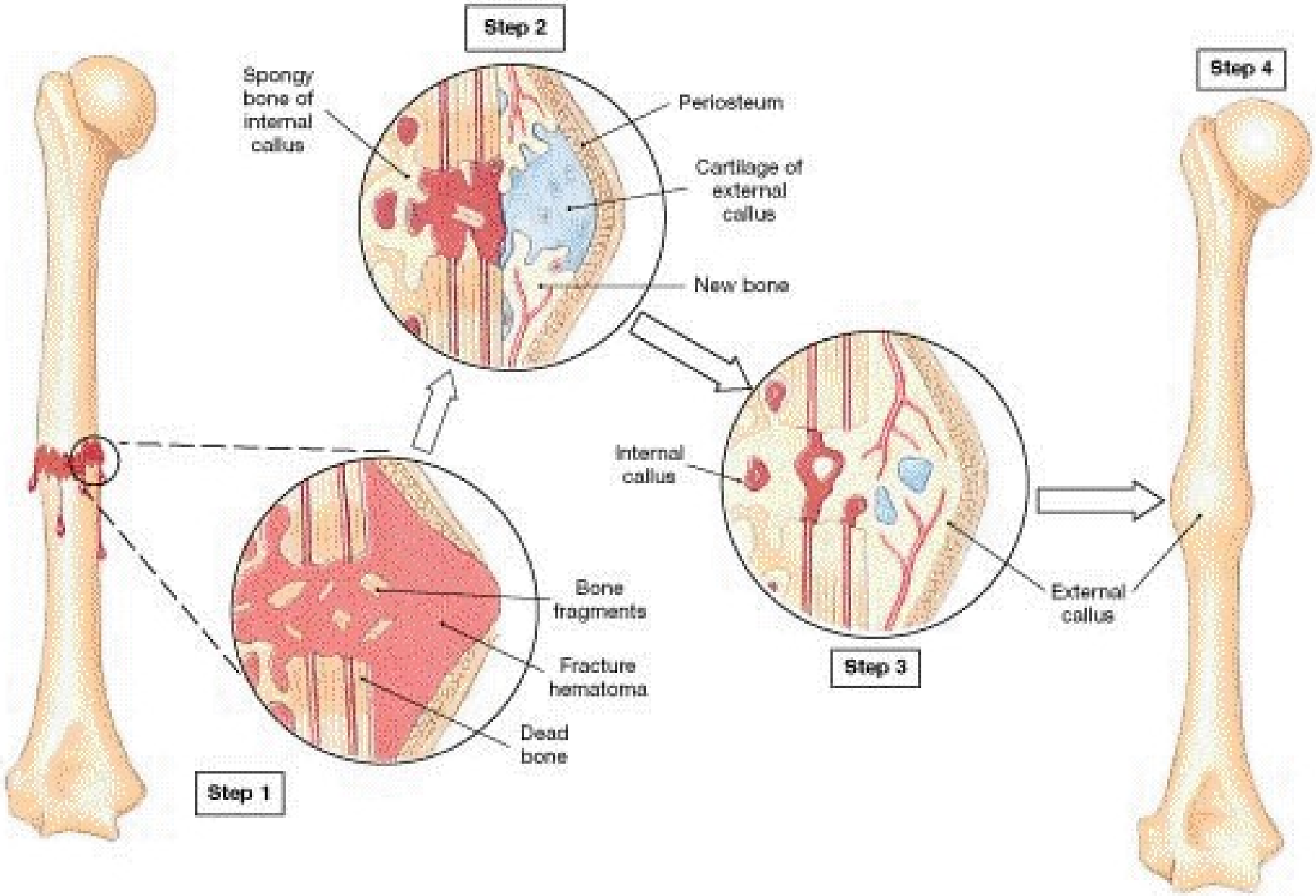
② **Fibrocartilaginous callus formation**



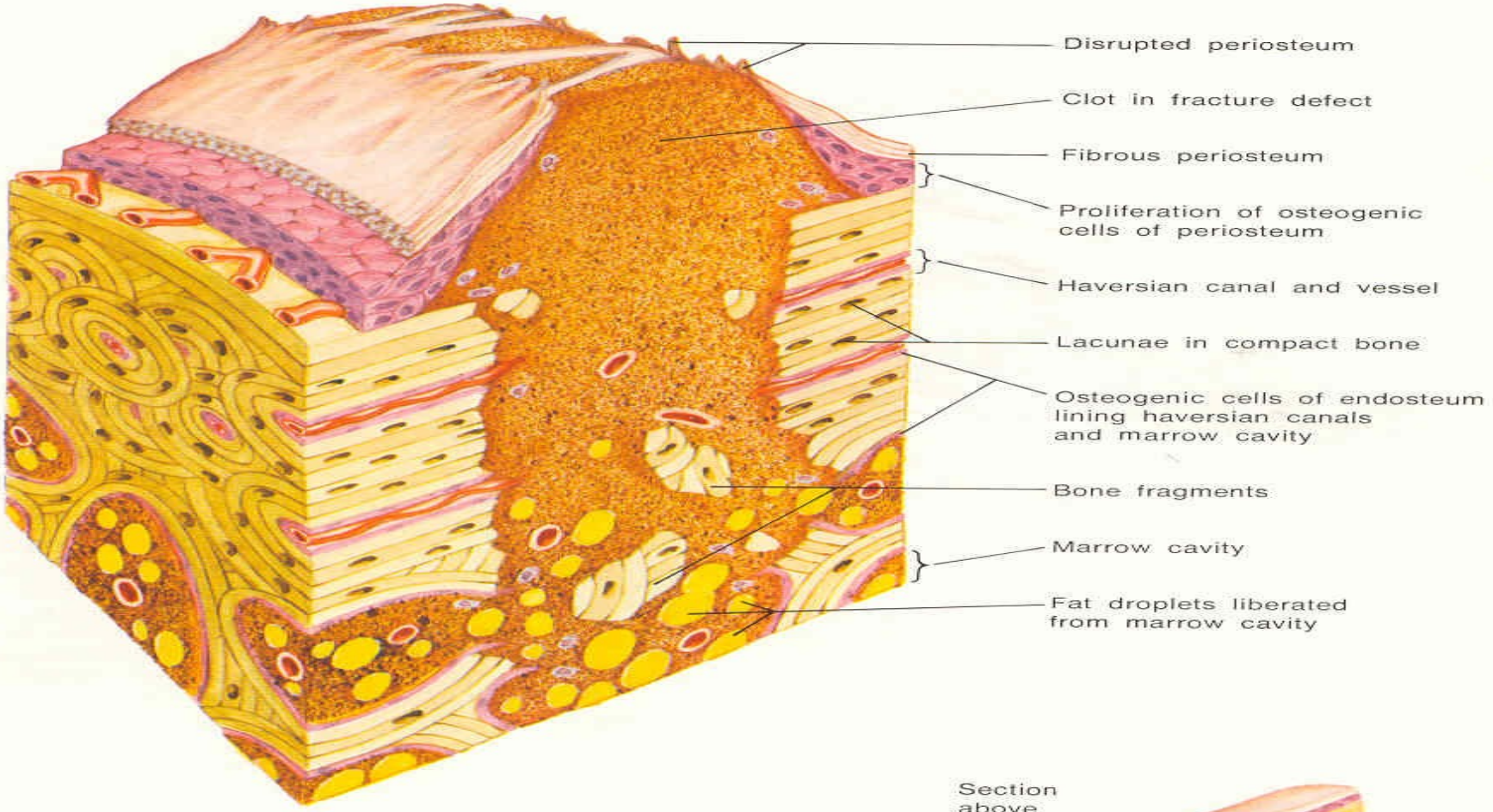
③ **Bony callus formation**

④ **Bone remodeling**

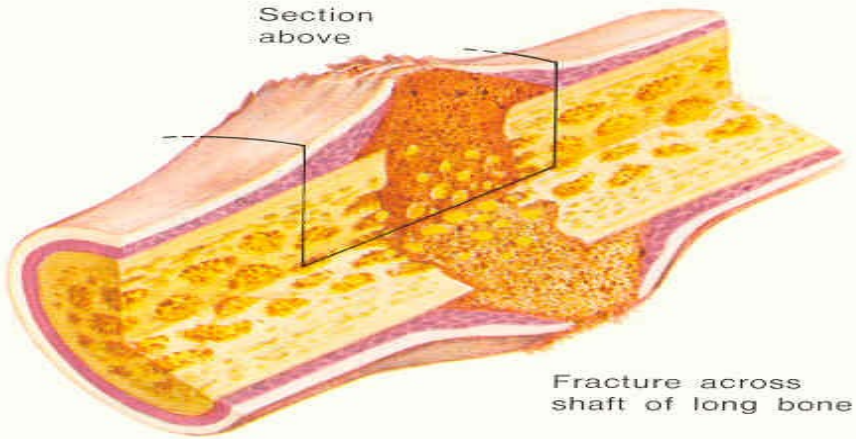
FIGURE 6-15 Steps in the Repair of a Fracture



Bone Repair (Early Phase)



Subsequent to an initial inflammatory response, early stages of bone fracture repair involve proliferation of osteogenic cells of periosteum and of endosteal lining of haversion canals and marrow cavity. These cells differentiate into chondroblasts, which form cartilaginous callus; osteoblasts, which form new bone; and osteoclasts, which resorb dead bone and bone fragments. Periosteal reaction extends beyond the immediate fracture site



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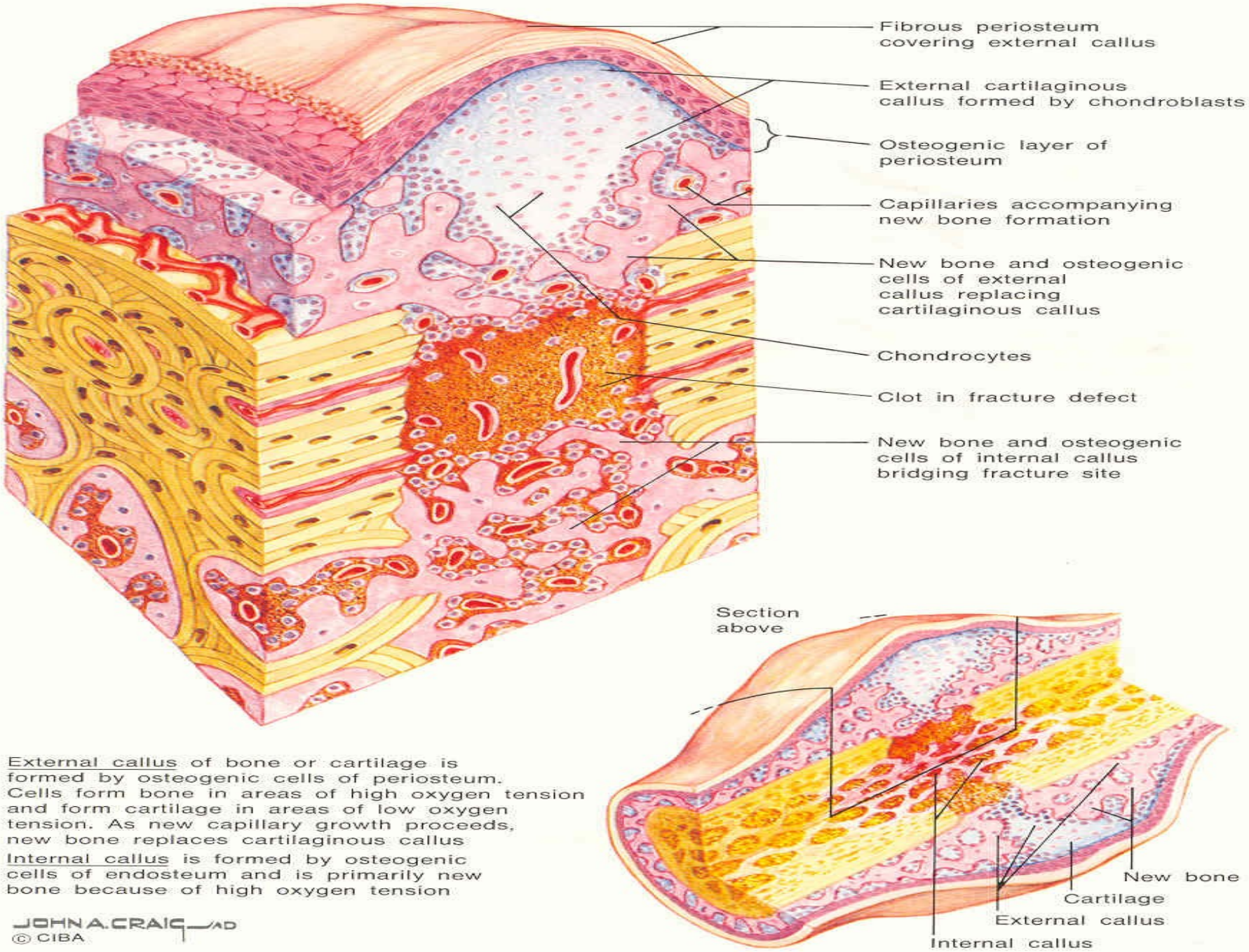
Bone Repair (Intermediate Phase)



External callus of bone or cartilage is formed by osteogenic cells of periosteum. Cells form bone in areas of high oxygen tension and form cartilage in areas of low oxygen tension. As new capillary growth proceeds, new bone replaces cartilaginous callus

Internal callus is formed by osteogenic cells of endosteum and is primarily new bone because of high oxygen tension

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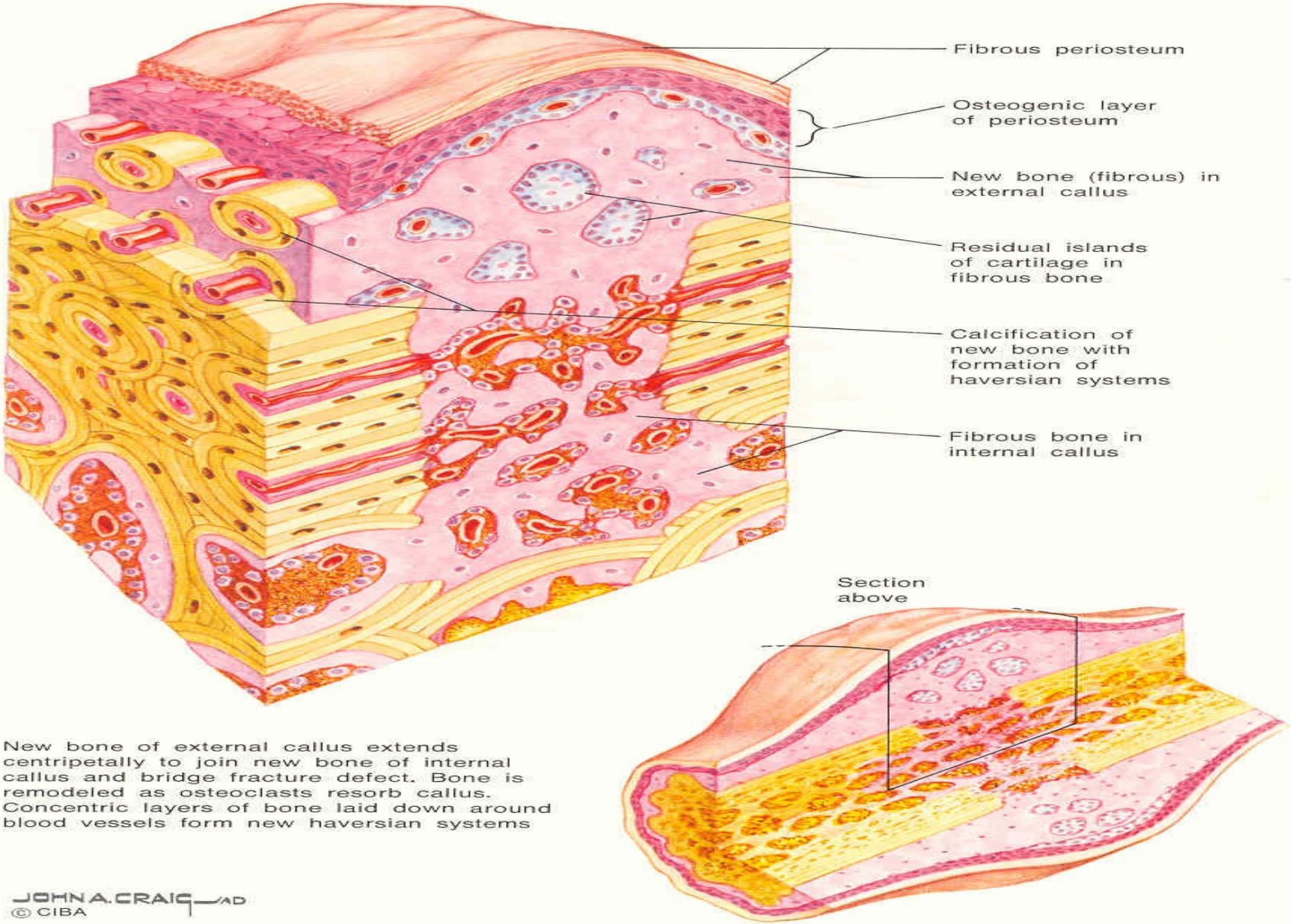
Bone Repair (Late Phase)



New bone of external callus extends centripetally to join new bone of internal callus and bridge fracture defect. Bone is remodeled as osteoclasts resorb callus. Concentric layers of bone laid down around blood vessels form new haversian systems

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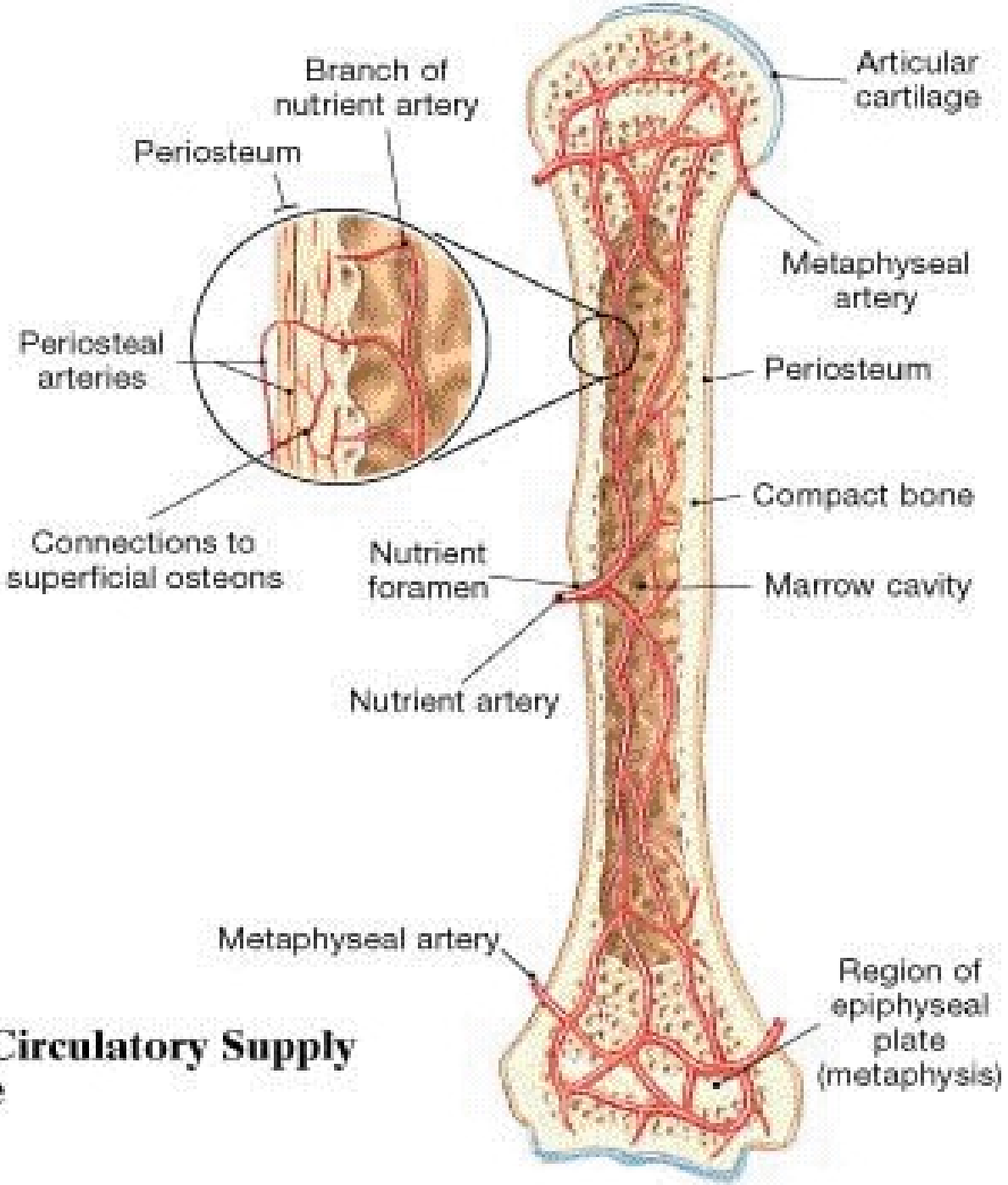


FIGURE 6-12 Circulatory Supply to a Mature Bone

OSTEOPOROSIS

- Osteoporosis, or porous bone, is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures of the hip, spine, and wrist.

Osteoporosis

New Trends in
Prevention and Treatment

Osteoporosis

- "A systemic skeletal disease characterized by low bone mass and microarchitectural deterioration, with a consequent increase in bone fragility with susceptibility to fracture."*
- Bone density ≥2.5 SD below young normal mean†

*Consensus Development Conference: Diagnosis, prophylaxis, and treatment of osteoporosis, *Am J Med* 1993;94:646.

†Kanis JA et al, *J Bone Miner Res* 1994;9:1137.

Fracture Risk in Women with Bone Density of –2.5 SD

Age (yr)	1-Year Risk (%)		5-Year Risk (%)	
	Hip	Any Fx	Hip	Any Fx
50	1	2	5	10
60	1.2	3	6	15
70	2	6	10	18
80	4	11	20	55

Fx = fracture

Suman VJ et al, *Bone* 1993;14:843. Hui SL et al, *J Clin Invest* 1988;81:1804.

Why Recognize & Treat Osteoporosis?

To Prevent Fractures!

- 1.5 million fractures/yr
- $10 billion direct costs
- 300,000 hip fractures/yr
  - 20% die
  - 25% confined to long-term facilities
  - 50% long-term loss of mobility

Risks for Osteoporosis

In young women

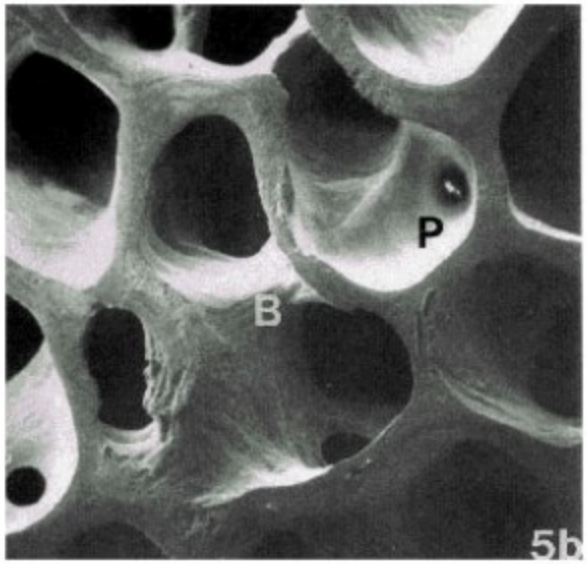
- Low calcium intake
- Low body weight
- Limited exercise
- Hypoestrogenism

In others

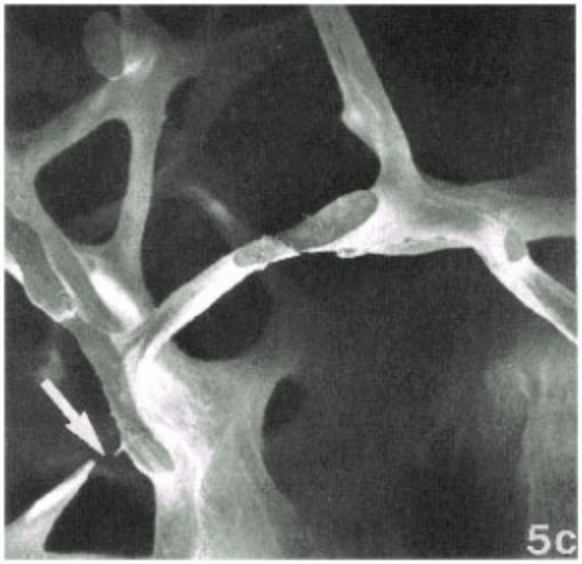
- Menopausal/postmenopausal status—without HRT
- Cigarette smoking
- Low-trauma fractures
- Hyperparathyroidism
- Chronic corticosteroid use

Normal & Osteoporotic Bone Architecture

Normal Bone

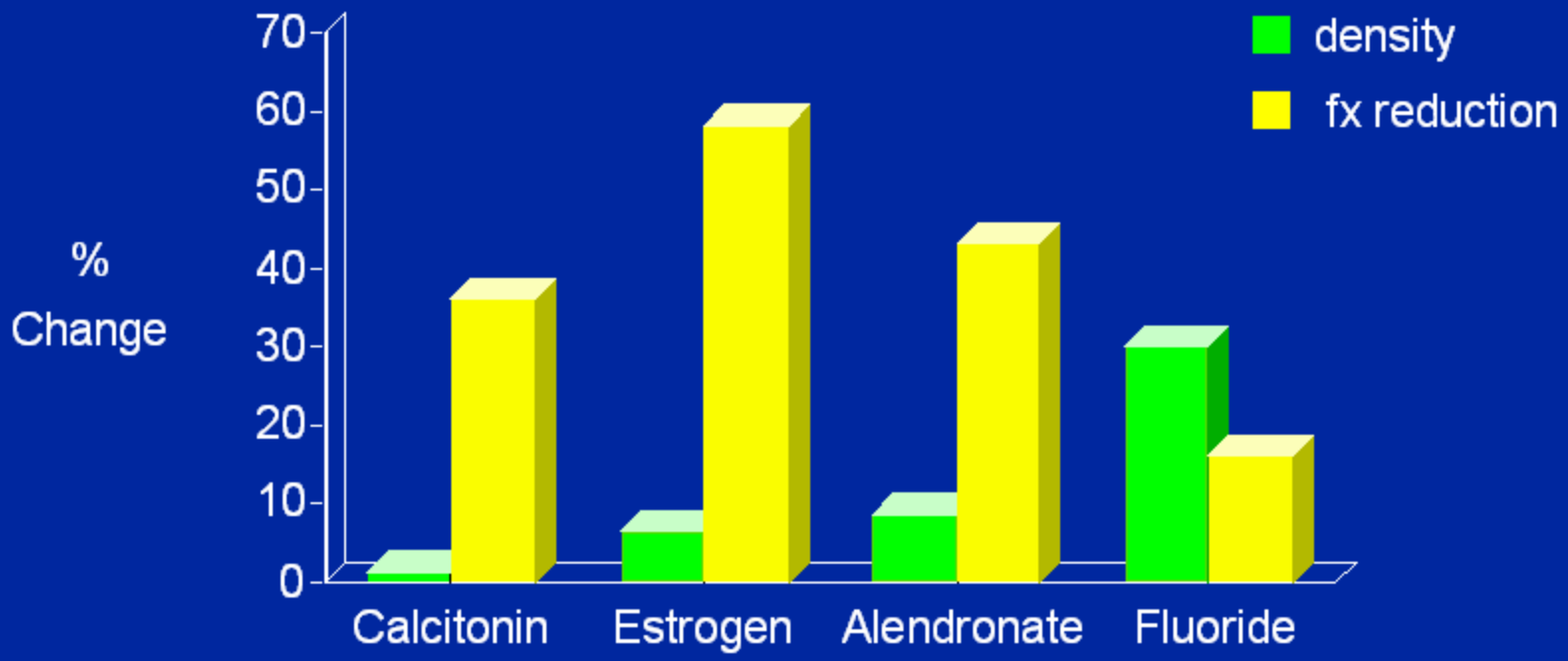


Osteoporotic Bone



Reproduced from *J Bone Miner Res* 1986;1:15-21 with permission of the American Society for Bone and Mineral Research. © 1986 by Massachusetts Medical Society. All rights reserved.

Therapeutic Comparisons



Biochemical Markers of Bone Formation and Resorption

Not Yet Clinically Confirmed

- Circadian rhythm in bone metabolism causes markers to vary by 10%–20%
- Urine creatinine varies during the day by 20%
- Urine crosslinks/creatinine ratios vary by 20%–30%
- Baseline and follow-up tests needed to draw conclusions. Change >30% is significant
- Large overlap in normal and osteoporotic women

Why Estrogen?

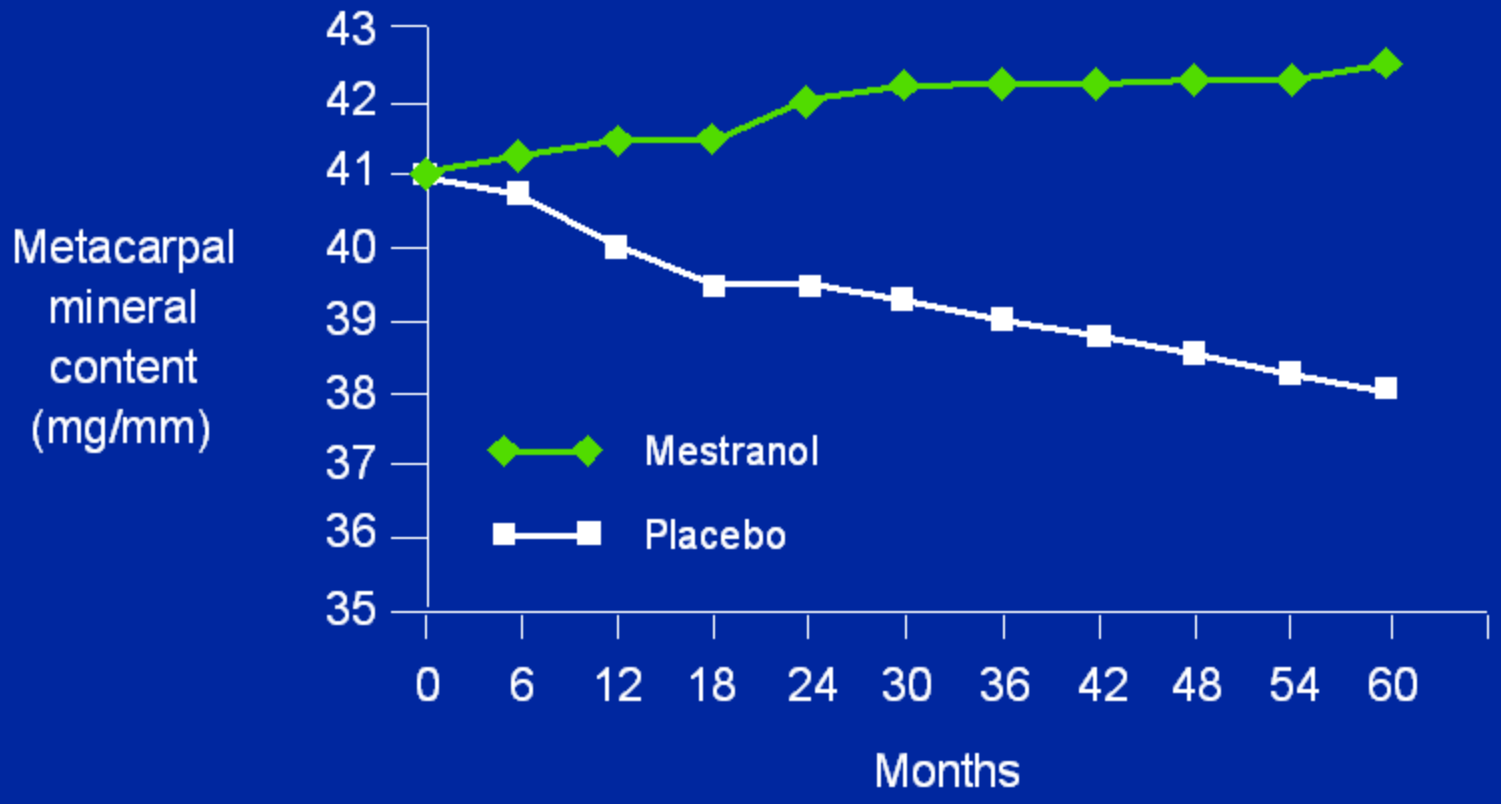
- Bone loss begins with menopause
- Bone loss is prevented or arrested by estrogen
- Estrogen is superior to calcium alone and exercise alone*
- Estrogen-deficient adolescent girls have reduced bone density

*Calcium and exercise should be a part of the therapeutic regimen.

Other Benefits of Estrogen

- Relief from hot flushes
- Improved sleep
- Relief from vaginal dryness
- Possible protection from Alzheimer's disease
- Decreased risk of cardiovascular disease

Long-Term Effects of Estrogen and Estrogen Depletion on Bone



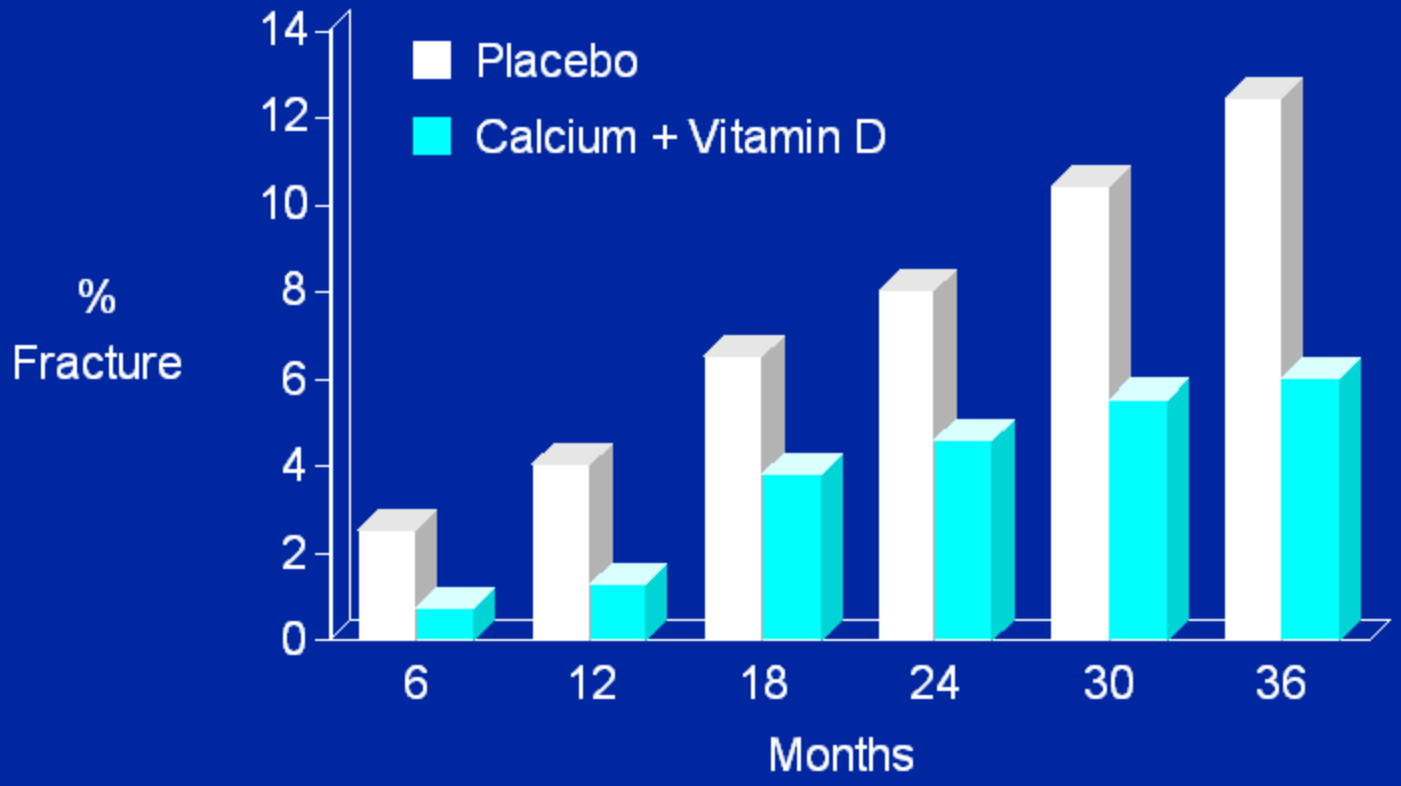
Lindsay R et al, *Lancet* 1976 May 15;1(7968):1038. © by The Lancet Ltd 1976. Reprinted with permission.

Risks of Estrogen Replacement

- Potential risk of breast cancer (prescribe estrogen with caution in women with history of breast cancer)
- Abnormal uterine bleeding
- Endometrial hyperplasia
- Migraine headaches in susceptible women
- Deep venous thrombosis*

*This risk is eliminated by the use of transdermal estradiol.

Reduction of Nonvertebral Fracture with Calcium and Vitamin D



p=0.02

Dawson-Hughes B et al, *N Engl J Med* 1997;337:670.

Cost Effectiveness of Treating Osteoporosis with HRT

Cost per year of life gained

- $24,000 in 1980 dollars
- $14,620 in 1990 dollars*
- $21,600 in 1995 dollars

*Treating only patients with low BMD.

Summary & Conclusions

1. Osteoporosis is a *preventable* disease — not a "condition of aging."
2. Persons at risk can be identified.
3. Technology for accurate bone density measurement exists.

(cont'd)

Summary & Conclusions (cont'd)

4. Estrogen is the agent of choice for prevention and treatment of postmenopausal osteoporosis.
5. Alternatives for women who cannot take estrogen include:
   a. Alendronate and other bisphosphonates
   b. Raloxifene and other SERMs
   c. Calcitonin

QUESTIONS

Fast Facts on Osteoporosis

- *Prevalence* - Twenty-five million Americans are affected by osteoporosis, making it a major public health problem.

- 80% of those affected by osteoporosis are women.

Fast Facts on Osteoporosis

- One out of every two women and one in five men have an osteoporosis-related fracture.
  - By age 75, one third of all men will be affected by osteoporosis.

Fast Facts on Osteoporosis

- Osteoporosis is responsible for 1.5 million fractures annually, including:
- · more than 300,000 hip fractures
- · 500,000 vertebral fractures
- · 200,000 wrist fractures
- · more than 300,000 fractures at other sites

Fast Facts on Osteoporosis

- *Risk Factors* - Certain people are more likely to develop osteoporosis than others. Factors that increase the likelihood of developing osteoporosis are called "risk factors." The following risk factors have been identified:
  - Being female
  - Thin and/or small frame
  - Advanced age
  - A family history of osteoporosis

Fast Facts on Osteoporosis

- *Risk Factors -*
  - Early **menopause**
  - Abnormal absence of menstrual periods (amenorrhea)
  - Anorexia nervosa or bulimia
  - A diet low in calcium
  - Use of certain medications, such as corticosteroids and anti-convulsants

Fast Facts on Osteoporosis

- *Risk Factors -*
  - Low testosterone levels in men
  - An inactive lifestyle
  - Cigarette smoking
  - Excessive use of alcohol
  - Caucasian or Asian, although African Americans and Hispanic Americans are at significant risk as well

Fast Facts on Osteoporosis

- *Risk Factors* - Women have approximately 10 to 25 percent less total bone mass at maturity than men, making them more susceptible to osteoporosis.
- However, five million American men are affected by osteoporosis and one out of eight men age 50 and older will develop fractures.

Fast Facts on Osteoporosis

- *Risk Factors* - White women 60 years of age or older have at least twice the incidence of fractures as African-American women. However, one out of five African-American women are at risk of developing osteoporosis.

Fast Facts on Osteoporosis

- *Cost* - In 1987, the estimated national direct expenditures (hospitals and nursing homes) and indirect expenditures (lost eamings) for osteoporosis and associated fractures was $10 billion ($27 million each day)— and the cost is rising.

Fast Facts on Osteoporosis

- *Symptoms* -Osteoporosis is often called the "silent disease" because bone loss occurs without symptoms. People may not know that they have osteoporosis until their bones become so weak that a sudden strain, bump, or fall causes a fracture or a vertebra to collapse. Collapsed vertebra may initially be felt or seen in the form of severe back pain, loss of height, or spinal deformities such as stooped posture or dowager's hump.